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Organization Is Bringing about a Peace Conference between the Retailer, Wholesaler and Manufacturer and Is Making Commercial War Indefensible, because Coöperation Is Taking the Place of Competition. Competition Is the Life of All Activities until It Becomes Destructive.

Vol. XXIII, No. 10 OCTOBER, 1934

JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

TRADE MARK

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THE 83rd ANNUAL MEETING OF THE AMERICAN PHARMACEUTICAL ASSOCIATION WILL BE HELD IN PORTLAND, ORE., IN 1935.

The 1935 Meetings of the American Association of Colleges of Pharmacy, the National Association of Boards of Pharmacy, Conference of Pharmaceutical Association Secretaries, of the Pharmaceutical Law Enforcement Officials and the Plant Science Seminar will also be held in Portland.

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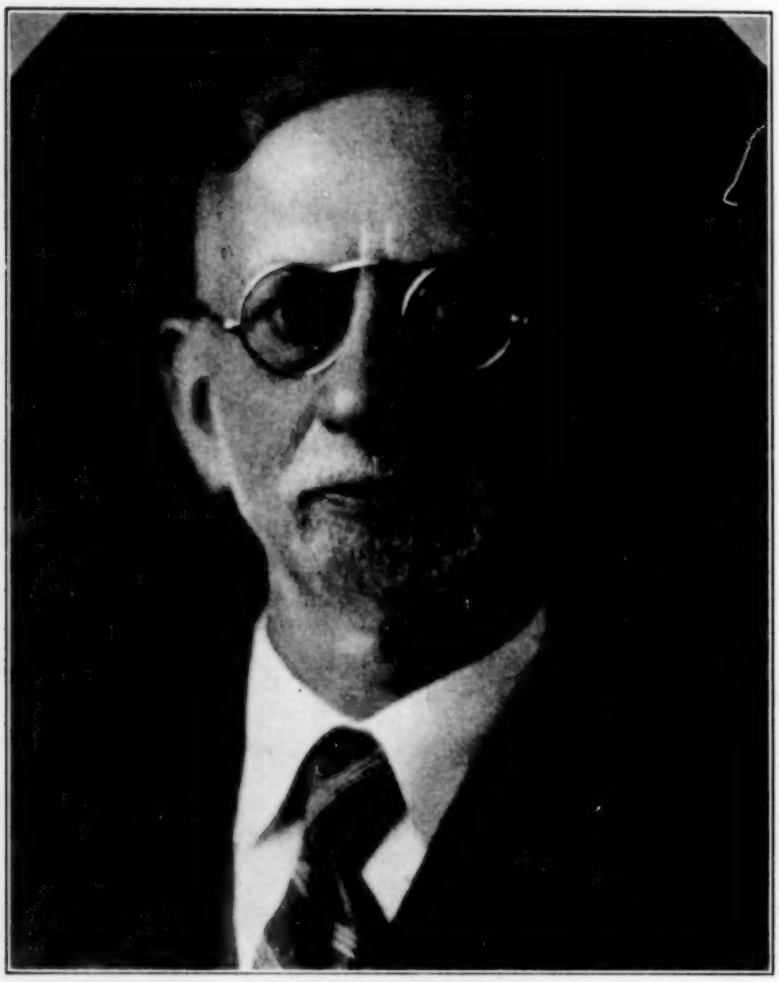

GEORGE A. GORGAS.

JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

VOL. XXIII OCTOBER, 1934 No. 10

GEORGE A. GORGAS.

This is the fiftieth anniversary of membership in the AMERICAN PHARMACEUTICAL ASSOCIATION of George Albert Gorgas. Mr. Gorgas was born in Cumberland County, Pennsylvania, November 1858; he received his early education in the public schools and the Cumberland Valley State Normal at Shippensburg, Pa., and thereafter served an apprenticeship in the pharmacy of Daniel H. Hamaker in Harrisburg. In 1879 he matriculated at the Philadelphia College of Pharmacy and graduated in 1881.

In 1883 Mr. Gorgas engaged in business on his own account, purchasing the pharmacy of I. D. Lutz on Market Square, Harrisburg; here he conducted the establishment until 1893, when he moved to the present location; later he opened two branch stores, one of which was discontinued last year.

The subject of this brief sketch has always shown interest in improving pharmaceutical practice for service of the public; he has been active in organization work and an outstanding member of the Pennsylvania Pharmaceutical Association, of which he was president in 1906; one of his presidential recommendations established Life Membership; in 1918 he was elected a Life Member and, this year, in recognition of his many services to pharmacy and years of loyal membership, he was elected an honorary member of that organization; he is also a member of the National Association of Retail Druggists.

In 1932 the Philadelphia College of Pharmacy and Science conferred on him the degree of Master of Pharmacy; he is a member of the Board of Trustees of that institution, and its "Model Pharmacy" was made possible through the efforts of Mr. Gorgas.

Our fellow-member is active in civic affairs, Kiwanis Club and Masonic bodies.

EDITORIAL

E. G. EBERLE, EDITOR 2215 Constitution Ave., WASHINGTON, D. C.

THE PHARMACY EXHIBIT—A CENTURY OF PROGRESS INTERNATIONAL EXPOSITION.

PHARMACY Week brings the message of pharmacy to the public each year, the Pharmacy Exhibit, in Chicago, brought its service to the attention of millions of visitors and the American Institute of Pharmacy, as the permanent home wherein the activities of pharmacy will be of record, acquaints the Government and the people that pharmacy has a most important part in standardizing materia medica and preparations in which these products are properly represented.

The Pharmacy Exhibit will be closed at the end of this month but it will be made permanent so that the purpose so successfully established will be continued.

In conformity with the general plan of A Century of Progress the Pharmacy Exhibit was arranged to appeal to the layman and under the direction of Chairman H. C. Christensen and the committee having the arrangements in charge the exhibit successfully met the test, attracted the interest of the visitors and received general favorable comment from them. The success was made possible through the coöperation of all divisions of pharmacy and the publicity given by pharmaceutical publications. In a dramatic manner visitors were told of the development of pharmacy and the use of drugs and the methods of standardization, so that they received a better understanding of the progress made educationally and otherwise in pharmaceutical service. The efforts of those in charge were supplemented by the schools of pharmacy, boards of pharmacy, revision committees of the U. S. Pharmacopœia, National Formulary and Syllabus, organizations, and the manufacturing industries—to all of them much credit is due.

The Exhibit portrayed the history of pharmacy, development of education and legislation—the purpose being to acquaint the visitors with the history of pharmacy, the progress made by contrasting old methods with new, showing the advances in educational and legal requirements, resulting in improved pharmaceutical service and protection of the public.

A comment on the activities of those in charge of the exhibit was made in the February JOURNAL and reference is made here to render credit for the accomplishment which marks a most important effort in the history of American pharmacy. In summing up, it may be repeated that the entire panorama of the exhibit informed the public of the great improvement in pharmaceutical service during the past century, from the crude products and utensils of the past to the uniform, standardized products of to-day with precision instruments and equipment; from the unsupervised practice of the past to the restricted and supervised practice of to-day, thus guarding the public health and welfare; from the pharmacist of yesterday to the one of to-day, equipped for research as well as practice.

The exhibit has been of benefit in bringing pharmacy's message to the general public and has had a distinct educational value for the professional man as is evidenced by the many registrations. A very favorable impression has been given to the medical and dental professions and pharmacy has risen in prestige. The pharmacist who has seen the exhibit has learned something more about his

profession and has come away with greater respect for it. These are not idle theories; they are the judgments expressed by the many visitors in conversations with attendants. Pharmacy has responded to an opportunity and profited thereby—the Pharmacy Exhibit and A Century of Progress have been eminently successful.

DECENNIAL OF PHARMACY WEEK.

THE thought which prompted and resulted in the annual celebration of Pharmacy Week was presented in the address of Robert J. Ruth, as chairman of the Section on Practical Pharmacy, A. PH. A., at the Buffalo meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION.

The underlying motive of a National Pharmacy Week is the education of the public relative to the mission and service of pharmacy, and any other purpose that will detract and confuse does not represent the idea which was uppermost in the mind of the founder of this annual occasion.

The earlier celebrations were directed by Robert J. Ruth and since by Anton J. Hogstad, Jr. The educational efforts of the latter and of E. L. Newcomb have brought pharmacy to the attention of schools and libraries by the series of maps—drug map of the World, chemical map of North America, map of pharmacy institutions and those engaged in educating and training pharmacists. The publications have whole-heartedly given support and directed the thoughts of pharmacists relative to ways that will bring the message of pharmacy to the public. All of the publications have contributed to the better understanding of pharmacy by the public; some have served in a larger way and these, no doubt, have been rewarded accordingly by the appreciation of those whose aim is to advance the profession.

The associations—local, state and national—have aided in the cause according to their opportunities and thereby their organizations and their members have gained by recognition of the professional standing that pharmacy enjoys. It remains for them to exhibit a greater interest, year by year, in order to make Pharmacy Week what it should be and to bring the message of pharmacy to the public in daily efforts through publicity of a high order, associating the service to a greater extent with matters that concern public health.

In an earlier editorial it was said, in substance, that science had added years to the span of human life and improved hygienic conditions—pharmacy as a profession, as a science and in its business relations contacts with the public and thereby Pharmacy Week summarizes the daily efforts of pharmacists. In years gone by drug stores were factors in the dissemination of news and formulating of plans far-reaching in their influence; to-day pharmacists have great opportunities for dissemination of public health information. What is needed is more publicity for pharmacy, more druggists who will actively express loyalty to pharmacy by doing their part and not letting others do it for them; those who have had an active part in Pharmacy Week have shown their loyalty by publicity which extends beyond the activities of the seven days so designated.

Canon H. J. Cody, formerly Minister of Education for Ontario, in addressing the recent convention of the Ontario Retail Druggists' Association said to the members:

"You are all, I am quite sure, prepared to regard yourselves primarily as ethical and scientific pharmacists. Perhaps the term 'Druggist' has in some quarters become usual, but to my mind, the term 'Pharmacist' is undoubtedly a term most suitable for application to the ethical and scientific side of your calling. Your work does require a broad foundation, not only of general knowledge, but of specific training. It is not fair, in these days, for anybody to serve the public unless his outlook is unduly wide, and his knowledge of the basic principles of his calling correctly based."

Referring to Pharmacy Week in his presidential address President R. L. Swain said: "Pharmaceutical legislation, pharmaceutical education, the whole of pharmaceutical service rests upon the professional character of pharmacy. Pharmacists should be keen to recognize this, and diligent in their efforts to impress it upon the public mind. I cannot be too emphatic in urging pharmacists to embrace every opportunity to advance and elevate their professional work as a basic and fundamental thing. The principles underlying it are sound, and the whole idea is a dignified and worth-while approach to a most important subject."

FORTY-EIGHT LABORATORIES.

BY ROBERT P. FISCHELIS.*

WHILE researches in chemistry, pharmacology and other medical and pharmaceutical sciences are being carried on with satisfactory progress in the laboratories of our colleges, research foundations and industrial establishments, other forms of research which profoundly affect the welfare of pharmacy and pharmacists are being neglected to some extent because of a lack of coördinated effort. In the forty-eight states of our Union, forty-eight legislatures are passing statutes intended to regulate various activities for the welfare of the people as a whole. Forty-eight Governors are issuing executive orders and directions for carrying out "the will of the people" as expressed in the legislative enactments of their representatives. Forty-eight State health departments are enforcing forty-eight State health laws with varying provisions which include regulation of the manufacture and distribution of foods and drugs. Forty-eight boards of pharmacy are enforcing forty-eight different pharmacy laws according to the powers conferred upon them to protect the public against incompetent prescription compounding and careless dispensing of drugs, medicines and poisons.

Undoubtedly, greater uniformity in these legislative and administrative activities is a desirable end. Yet there is also an advantage in lack of uniformity. Under our system of government the forty-eight states are really forty-eight laboratories in which a great variety of experiments can be carried on with much profit and advantage to the people as a whole. As a matter of fact, State food and drug laws, and laws for the regulation of traffic in narcotic, hypnotic and other

* President, AMERICAN PHARMACEUTICAL ASSOCIATION.

deleterious or poisonous drugs have preceded and paved the way for federal regulation along similar lines. The State laws have shown the weakness of some methods of regulation and the strength of others. It is not uncommon for one State or group of States to establish procedures which may be considered radical or extreme in one decade only to become the minimum standards throughout the Country in the next.

But to what extent is Pharmacy profiting by the researches and experimental developments in our forty-eight laboratories? Do the pharmacists of New York have any conception of what is going on in the profession in Oregon or do the members of the profession in Maine have available the results of regulatory experiments in the distribution of drugs and medicines or the public control of health matters in California? The answer is to be found in the multiplicity of outmoded and often unworkable proposals for regulation of various phases of the practice of pharmacy which crop out annually in every State when officers and committees are assigned to accomplish a progressive revision of unsatisfactory existing conditions.

There appears to be no central agency to which pharmacists in the forty-eight states can turn to-day for summarized information as to what has been tried and found wanting or what has been tried and found effective. This does not mean that the information cannot be had, for it certainly exists. However, it is locked within the borders of individual states and frequently it can be had only through personal contact with individuals because no one has taken the trouble to record what months and even years of patient effort may have brought about.

The Conference of Pharmaceutical Law Enforcement Officials is the brightest spot that has appeared on the horizon for some time as far as the coördination of legislative and law enforcement information is concerned. The Conference of Pharmaceutical Association Secretaries is moving in the direction of providing a valuable interchange of information on State Association activities. Both groups have been stimulated and encouraged by the AMERICAN PHARMACEUTICAL ASSOCIATION.

However, these agencies as well as the National and State organizations representing the various subdivisions of Pharmacy, require the services of a clearing house where the results of surveys of local, State and National conditions may be recorded, digested and disseminated; where the results of pioneering researches in problems of social as well as technical and industrial significance to the profession may be collated and evaluated and from which sound bases for the development of pharmaceutical education and licensure and the control of the manufacture and distribution of drugs and medicines may emanate. A coördination of the experimental work of our forty-eight laboratories so as to avoid waste and duplication of effort will advance the cause of pharmacy tremendously. The coördinating agency or master laboratory should be set up in the Institute of Pharmacy of the AMERICAN PHARMACEUTICAL ASSOCIATION. Here is a specific project of benefit to pharmacy as well as to the people of our country for which funds must and should be advanced promptly. The National and State pharmaceutical associations could find no better common meeting ground on which to start coöperative work and give evidence of the sincerity of their expressed desire to advance the welfare of the profession.

SCIENTIFIC SECTION

BOARD OF REVIEW OF PAPERS.—*Chairman*, F. E. Bibbins, George D. Beal, L. W. Rising, H. M. Burlage, L. W. Rowe, John C. Krantz, Jr., Heber W. Youngken.

THE GUINEA PIG AS A HEMATOPOIETIC TEST ANIMAL.*

(A PRELIMINARY REPORT.)

BY J. W. LANDSBERG AND MARVIN R. THOMPSON.

Since the introduction of liver extract into clinical medicine, there has been the need of a dependable laboratory assay method to determine the potency of this therapeutic agent. There have been various methods of assay introduced (1, 2, 3) but the practicability and the specificity of these methods may be questioned. In two of the described methods, McGowan (1) and Vaughan, *et al.* (3), used the domestic fowl and the pigeon, respectively. In the other method, McGowan and Sinclair (2) used the domestic pig (*Sus scrofa*).

In a consideration of the first two methods, there are several factors worthy of mention. The erythrocytes of both the domestic fowl and the pigeon belong to the nucleated series. This fact detracts from the practicability of the methods due to the difficulty encountered in the enumeration of the reticulocytes. This difficulty was evidently experienced by Edmunds, *et al.* (4), as they state, in comparing their work to that of Vaughan (3), "This discrepancy may possibly be explained by the method of counting and classification" (page 92, par. 3).

The presence of a nucleus in the erythrocyte causes some difficulty in determining which cell is a reticulocyte and which is not, leaving the final decision to the judgment of the worker. This factor introduces a personal variation which may have considerable bearing upon the final result. When a non-nucleated blood sample is used this difficulty cannot arise. If the cell in question has a small or large amount of reticular material it is a reticulocyte and must be enumerated as such. The worker is not confused by the dual presence of a nucleus and a reticulum and is therefore able to differentiate, without personal influence, those cells which are reticulocytes and those which are not.

Another factor present in the published methods is that of housing the test animal. The average animal room does not readily lend itself to colonies of pigeons and domestic fowls. The confined area of the cages plus a reduced amount of sunshine and exercise must effect the general well-being of the animal. These conditions are rather far removed from the natural habitat of such animals. Peabody and Neale (5) make the following statement concerning this problem ". . . it was noticed that long confinement on the rather restricted diet apparently produced subnormal blood conditions" (page 1231, par. 2).

This difficulty also presents itself in the work of McGowan and Sinclair (2) who used the domestic pig (*Sus scrofa*) of about four months of age weighing about

* From the department of Pharmacology, School of Pharmacy, University of Maryland. Abstracted from a report presented before Scientific Section at the Annual meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION, May 7, 1934, Washington, D. C.

43.5 pounds. The difficulties of maintaining an animal colony of such test objects are easily discernible without further elaboration.

Previously suggested methods, in some cases, involve the use of an experimental animal with abnormal blood conditions. Some investigators (1, 2, and 5) have used experimental animals suffering with various degrees of anemia. Such circumstances we feel must certainly create a marked variation in the response of the test animal to the therapeutic agent. As these anemias are present because of pathological conditions and are not produced by controlled artificial methods, the degree of anemia will vary from time to time in the same animal and will certainly differ in a group of animals. The degree of anemia present, accompanied by the changes in the hematopoietic organs, and the efforts of the hematopoietic system to regenerate red blood cells must certainly influence the response produced by liver extract. It is certainly possible and not highly improbable that the same dosage of liver extract would produce a greater reticulocyte response in a hematopoietic system in need of such a stimulant than in a normal one which did not, provided of course, that the blood-producing organs were not partially or completely exhausted.

The present study was undertaken to find a normal, healthy experimental animal meeting the following requirements: (1) having non-nucleated erythrocytes; and (2) thriving under the usual animal room environment. We selected the guinea pig because it satisfied these two requirements and also because of the facility with which we could obtain the blood smears from the marginal veins of the ears of this animal. It was our purpose to determine whether or not a normal, healthy guinea pig would give a reticulocyte response to liver extract and still remain essentially normal.

These studies represent a preliminary endeavor to determine the practicability of using the guinea pig as a hematopoietic test animal and they should be followed by a more elaborate and comprehensive study.

METHODS.

General.—The guinea pigs were selected without reference to particular breed. Normal, healthy, adult pigs, of male sex, were chosen. The weight range was between 500 and 800 Gm. The diet, upon which these pigs had been maintained and which had proved adequate, was not modified during the experiment. Before an animal was used for experimental purposes an erythrocyte count and a blood smear were made to determine whether or not the blood of the animal was normal. Reticulocyte counts were determined on each animal to be studied to establish a normal base line. The animals were weighed before injection, several times during the injection period, and after the injection period. Erythrocyte counts were made before, during and after the period of injection. The incisions on the marginal veins were very small so as not to cause excessive bleeding which might result in a hemorrhagic anemia. During the routine procedure the animal lost only two small drops of blood per day; in some few instances perhaps four or five drops, but at no time was the blood loss sufficient to cause an anemia, as will be demonstrated in the discussion. The first drop of blood obtained was discarded and the second drop used for the reticulocyte enumeration. The subcutaneous injections were given over a period of eight consecutive days. The smears, made every day at approximately the same hour, were immediately followed by the injections.

Hematological Methods.—The ear was incised on the marginal vein and a small drop of blood was placed on a chemically clean cover-slip. With a sharpened toothpick a drop of alcoholic brilliant cresyl blue was added to the blood on the cover-slip. The blood and stain were mixed intimately with the toothpick, the second chemically clean cover-slip was placed over the first

and the blood allowed to spread. The smear was then pulled, the two cover-slips were allowed to dry in the air, and counterstained with Wright's stain.

In the enumeration of the reticulocytes five hundred red cells were counted in consecutive fields. The portions of the slides selected were thin and evenly spread in order that the red cells would not overlap. The reticulocyte count was made with oil immersion and the field reduced so that not over twenty-five red cells were counted per field. If the smear was at all difficult to count, one thousand red cells were examined. The reticulocyte counts were made by one person throughout the experiments. Some of the smears (containing the higher percentages of reticulocytes) were sent to a technician, trained by one of the authors, for a reticulocyte count. The technician did not know the reticulocyte count and, in fact, was not aware of the investigations being carried on by us. In all instances our reticulocyte count did not vary over one per cent from that of the technician.

The red corpuscles were counted in a new Newbauer Counting Chamber using the Thomas red cell pipette. Both of these instruments were certified by the Bureau of Standards. The average of two red counts, the difference between the two being not over one hundred thousand, was taken as the red-cell determination.

Dosage.—The experimental animals were injected with 1 cc. (per day) of No. 343 Lilly Liver Extract[1] at approximately the same hour each day. As the liver preparations were injected subcutaneously in the abdominal region, great care was exercised not to penetrate the abdominal wall and expel the fluid into the visceral cavity. With one exception, all the animals received the same dosage of liver extract over the same period of time (eight days). (This animal received extract for one day longer than the other animals, and 2 cc. of extract for the last two days.) One cc. of the extract was stated to be equivalent to five Gm. of liver. Each animal, therefore, received a total equivalent of 40 Gm. of fresh liver. We have reason to believe that smaller doses will produce satisfactory responses.

RESULTS AND DISCUSSION.

Control Periods.—As a control measure, each animal was observed for a period of about seven days before it was injected with liver extract. During this time the reticulocytes and the erythrocytes were counted and the animal weighed. The normal averages for reticulocytes ranged from 0.63 per cent to 3.54 per cent (Table I).

Effect of Iron on Reticulocyte Response.—It was essential to ascertain if the method used was producing a post-hemorrhagic anemia through blood loss. If the method was producing an anemia, there should be a definite response to iron and ammonium citrate which is used clinically for post-hemorrhagic anemia. On the other hand, if no anemia was produced by the puncture of the marginal veins, but a reticulocyte response occurred as the result of iron present in the extract, this also could be demonstrated.

For this experiment two pigs were used and subjected to the same method of procedure. Normal findings were recorded for five days and the average of these used as a base line. A solution of iron and ammonium citrate (U. S. P.) was made with distilled water of such strength that one cubic centimeter of the solution contained 2.5 mg. of iron and ammonium citrate. The solution was given as described under "DOSAGE." The experimental animals were injected every day for eight days. The reticulocyte counts were made during this period and for nine days following the injection interval to provide for a delayed response. Neither the reticulocyte count, the erythrocyte count nor the weight was influenced by the iron and ammonium citrate.

[1] We are indebted to Dr. H. W. Rhodehamel, of the Eli Lilly Company, for generously supplying us with the liver extract preparations.

Following this procedure the pigs were left in their cages, under the same conditions as those preceding the experiment, for a period of one month. At the end of this interval the reticulocytes were counted on four successive days to obtain a normal range, and the injections of liver extract were begun. The injections were carried on for eight days. The liver extract produced a definite reticulocyte response (Table I, animals number 1 and number 2), but did not effect the erythrocyte count nor the weight.

As there was no response to the injection of iron and ammonium citrate, one may draw two conclusions: (1) that no anemia was produced by the hematological methods; (2) that the experimental animals were not suffering from a nutritional anemia. The hematopoietic system, in cases of post-hemorrhagic anemia, attempts to compensate for the blood loss without therapeutic stimulus which alone would have produced some reticulocyte response. As iron preparations are clinically recognized in the treatment of post-hemorrhagic anemias a response should have occurred if this condition were present. Schultze and Elvehjem (6) have demonstrated that iron (in the presence of copper) brought about a definite reticulocyte increase in conditions of nutritional anemia. Our experimental animals were obtaining sufficient copper from the diet to utilize any iron present, therefore a reticulocyte rise should have occurred if this anemia were present.

TABLE I.

Experimental. Animal No.	Reticulocytes. Normal Average.	Reticulocytes. Increase.	Reticulocytes. Percentage Increase.	Day of Maximum Increase.
1	1.05%	3.95%	376 ± 95	8
2	0.95%	3.85%	405 ± 105	9
3	1.70%	5.10%	300 ± 58	10
4	1.30%	4.10%	315 ± 76	11
3 (Reinjection)	0.63%	3.77%	598 ± 158	7
4 (Reinjection)	1.23%	4.17%	339 ± 81	10
5	3.30%	1.70%	51 ± 33	9
6	3.70%	4.50%	121 ± 27	5

Effect of Liver Extract on Reticulocyte Response.—The injection of liver extract produced a reticulocyte response in all the experimental animals tested (Table I) without an increase in the erythrocytes or the weight. After the peak of the response had been reached the number of reticulocytes gradually returned to normal. The question immediately arose as to whether the hematopoietic organs had been exhausted by such stimulation or whether they would again respond to liver extract. After a period of one month two experimental animals, previously used, were again injected, the same technique being used. There was a definite response to the liver extract (Table I, reinjection).

These studies are particularly interesting in that they point to the possibility of a standardized laboratory animal. If such is the case, one could not only determine the potency of a preparation, but also could compare directly the action of various preparations upon the same animal.

Effect of Heat on Liver Extract.—The liver preparations injected produced a significant rise in the reticulocyte count. With this fact in mind, we were desirous of determining what influence a modified sample of the preparation would produce.

The sample was prepared as follows: 16 cc. of the extract were rapidly boiled to dryness without scorching. To the residue was added enough distilled water to bring the volume to 16 cc.; this sample was again boiled to dryness and the residue dissolved in enough distilled water to make the volume 16 cc.

After the normal base line was obtained the same procedure of injection was carried out as in the previous experiments. The response produced by the injection of the heated sample was definite, but less than that created by the unmodified sample (Table I, animals number 5 and number 6). The heating did not destroy the activity, but may have reduced the potency somewhat. Additional study may clarify this point.

In Table I the reticulocyte responses following the injection of liver extract are given. The erythrocyte counts did not change significantly, and are therefore omitted to conserve space.

From the data thus far obtained, we feel that the method described compares favorably with the other methods presented in the literature and is, therefore, worthy of further study, particularly with reference to its specificity.

In a personal communication from Dr. H. W. Rhodehamel, of Eli Lilly and Co., we have learned that the samples of liver extract used had shown clinical activity.

CONCLUSIONS.

1. A method suggesting the possibility of using the normal, healthy guinea pig as a hematopoietic test animal is introduced.
2. Experimental test animals that did not respond to injections of iron and ammonium citrate later gave a reticulocyte response when injected with liver extract.
3. The injection of liver extract over a given period caused a definite rise in the reticulocyte count without significantly effecting the erythrocyte count or the weight.
4. A second period of injection produced a response in the reticulocyte count similar to that produced in the first period suggesting the possibility that a given animal may be repeatedly used for test purposes.
5. The active constituent of liver extract which produced a reticulocyte response in the guinea pig is not readily destroyed by heating.
6. This report is of a preliminary nature and is presented merely as a possibility worthy of further study.

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ALKALOIDAL REAGENTS V. THE ACONITE ALKALOIDS.*

BY JAMES C. MUNCH AND HARRY J. PRATT.

The reactions of the aconitine group of alkaloids with the usual alkaloidal reagents, as well as with certain special reagents reported in the literature, contain

* Scientific Section, A. Ph. A., Madison meeting, 1933.

conflicting statements regarding colors and precipitate formations (1–30). Data on aconitine, pseudoaconitine and benzoylaconine are given in Table I.

TABLE I.—REACTION OF ACONITE ALKALOIDS WITH ALKALOIDAL REAGENTS.

(Reported in the Literature.)

No.	Reagents. Name.	Composition.	Aconitine. Color or Ppt.	Threshold, Mg./Liter.	Pseudoaconitine.
1	.....	HCl conc.	Colorless	...	.....
2	.....	HNO_3 conc.	Colorless; heated, brick-red	...	.....
3	Vitali	HNO_3 + KOH alc.	Colorless; odor EtOBz	...	Purple-red
4	Alvarez	Br + HNO_3 + NaOH alc., then 10% aq. $CuSO_4$	Red or brown; deep green	...	.....
5	.....	H_2SO_4 conc.	Colorless	...	Colorless
6	Erdmann	H_2SO_4 + HNO_3	Colorless, changing to violet	...	.....
7	.....	H_2SO_4 + $K_2Cr_2O_7$	Yellow to light green	...	.....
8	Mandelin	H_2SO_4 + NH_4 meta-vanadate	Light brown to orange	...	.....
9	Froehde	H_2SO_4 + Na molybdate	Yellow–yellowish–brown–blue	...	.....
10	Mecke	H_2SO_4 + SeO_2	Yellowish; lt. brown on heating	...	.....
11	Marquis	H_2SO_4 + HCHO	Colorless	...	.....
12	Monti	H_2SO_4 + resorcinol	Yellow-red to red-violet	...	.....
13	Schneider	H_2SO_4 + sucrose	Red	...	.....
14	.....	Phosphoric acid conc.	Red; violet on heating	...	Colorless
15	.....	Phosphomolybdic acid	White; turning blue (A)	200	.....
16	Palet	H_3PO_4 + Na molybdate	Violet	...	.....
17	DeVry's-Sonnen-schein	NH_4 phosphomolybdate	Yellowish white ppt. (A)	...	.....
18	Scheibler	Phosphotungstic acid	White ppt. (A)	200	.....
19	.....	Phosphoantimonic acid	White ppt. (A)	1000	.....
20	Ecolle	Silicotungstic acid	White ppt. (A)	...	.....
21	Wormley	Br + KBr	.....	2	.....
22	.....	KBr	.....	10	.....
23	.....	HIO_3	Colorless	...	.....
24	Wagner	IKI[a]	Red, brown crystals	2	Precipitate
25	Jurgens	KI + CH_3COOH	Tabular rhomboids	50	Needle druses
26	Dragendorff	BiI_3.4KI	Yellow (A)	...	.....
27	Marme	CdI_2.2KI	Orange-red (A)	100	.....
28	Mayer	HgI_2.2KI	Yellowish white (A)	100	Ppt. dilute soln.
29	.....	$NaClO_4$	.....	2	.....
30	.....	$K_2Cr_2O_7$	Yellow ppt.	2	.....
31	Dunstan and Carr	$KMnO_4$	Dense purple-red crystals	250	.....
32	.....	Na or NH_4CNS	(A)	10	.....
33	.....	K_3FeCN_6	Ppt. conc. soln.	...	.....
34	Cole	K_4FeCN_6	Ppt. conc. soln. (A)	...	.....
35	Mellaneh	K_4FeCN_6 + HCOOH	Green	...	Green
36	.....	Na nitroprusside	(A)	...	.....
37	Fehling Solution	Alkaline copper compd.	Granular white ppt.	...	.....
38	.....	$AuCl_3$[a]	Whitish yellow (A)	200	Ppt. dilute soln.
39	.....	$PtCl_4$	Ppt. conc.	500	Ppt. conc. soln.
40	.....	$FeCl_3$	Yellow (A)	...	.....
41	.....	$HgCl_2$	Ppt. conc. (A)	...	.....
42	Millon	$HgNO_3$	White (A)	...	.....
43	.....	$AgNO_3$	(A)	10	.....
44	.....	$ZnCl_2$	(A)	...	.....
45	.....	$PdCl_2$	(A)	...	.....
46	.....	CH_3COOH	Red crystals	...	.....
47	.....	Gallic acid	Colorless	...	.....
48	Hager	Picric acid	Yellow concn. soln. (A)	250	.....
49	Knorr	Picrolonic acid	(A)	...	.....
50	Rosenthaler	Rufianic acid	(A)	5000	.....
51	.....	Tannic acid	.....	300	Ppt. dilute soln.
52	.....	$NaHCO_3$	Characteristic rosettes	10000	.....
53	.....	KOH	(A)	5000	.....
54	.....	KCN	(A)	5000	.....

[a] Benzoylaconine gives a yellow ppt. with $AuCl_3$ (38) and granular crystals with IKI (24).

A = Amorphous ppt.

The series of standard alkaloidal reagents used in our previous investigations (13, 19, 20, 21) were supplemented by a number of special reagents, a total of 71 being considered. Our results are given in Table II. Deviating somewhat from our previous practice, one drop of solution was placed on a watch crystal and mixed

TABLE II.—REACTIONS OF ACONITE ALKALOIDS WITH ALKALOIDAL REAGENTS.

No.	Reagent.	Aconitine.	Benzoylaconine.	Aconine.
1	HCl	0	0	0
2	HNO_3	0	0	0
5	H_2SO_4	0	0	0
6	$H_2SO_4 + HNO_3$	0	0	0
7	$H_2SO_4 + K_2Cr_2O_7$	0	0	0
8	$H_2SO_4 + NH_4$ meta-vanadate	Yellow soln.; large specks	Yellow soln; large specks	Yellow soln.; large specks
9	Froehde	Cold, 0; heated, 0	Cold, 0; heated, blue-gray	Cold, 0; heated, blue-gray
10	Mecke	0	0	0
11	Marquis	0	0	0
12	H_2SO_4 + resorcinol	Cold, 0; heated, lt. brown granules (A)	Cold, 0; heated, orange granules (A)	Cold, 0; heated, red-violet bundles of tabloids (C) ?
13	Schneider	Cold, 0; heated, black	Cold, 0; heated, black	Cold, 0; heated, black
55	H_2SO_4 + saccharose	Cold, 0; heated, brown	Cold, 0; heated, black	Cold, 0; heated, black
14	H_3PO_4	Red-violet	Black	Dark violet
16	Palet	Dark purple, changing to black	Red-purple, changing to dark brown	Purple-violet, changing to green, then dark green
18	Schiebler	Dense white (A)	Whitish yellow (A)	White (A)
20	Ecolle	Fluffy white (A)	Clabber white (A)	Curdy white (A)
56	$HNO_3 + Br$	0	0	0
23	$H_2SO_4 + KIO_3$	0	0	0
24	Wagner	Curdy light brown (A)	Staining; no ppt.	Dark brown (A)
26	Dragendorff	Dense white flocc. (A): later dark	Amorphous white ppt. and tables	Cloudy white (A)
28	Mayer	Dense white flocc. (A)	Sparse white warts (A)	Sparse white warts (A)
57	$KClO_3$	0	0	0
30	$K_2Cr_2O_7$	Yellow (A)	Yellow (A)	Yellow (A)
31	$KMnO_4$	Purple (A)	Purple (C)	Purple (C)
33	K_3FeCN_6	Green-white (A)	Green-white (A)	Green-white (A)
34	K_4FeCN_6	White granular (A)	Whitish yellow (A)	White granules (A)
35	Mellaneh	Greenish blue granules (A)	Greenish blue granules (A)	Greenish blue granules (A)
36	Na nitroprusside	White rods (A)	White (A)	White (A)
37	Fehling's soln.	White granules (C)	Sparse tablets (A)	Sparse tablets, bundles (C)
39	$PtCl_4$	Yellow white plates (A)	Yellow-white plates (A)	Yellow white plates (A)
40	$FeCl_3$	Yellow (A)	Sparse yellow (A)	Sparse yellow (A)
41	$HgCl_2$	Black (A)	Specks (A)	Gray (A)
42	Millon	White (A)	Soln., later white needles	White warts (A)
45	$PdCl_2$	Specks (A)	Lardy mass white (A)	Specks (A)
46	CH_3COOH	0	0	0
48	Picric acid	Dense yellow (A)	0	0
54	KCN	White (A)	Large tables (C)	Tables, prisms (C)
58	Dimethylglyoxine	Amorphous, later rods	Amorphous	Feathery sheaves
59	HCl + vanillin + Br	0	0	0
60	$HNO_3 + CuSO_4$	0	0	0
61	H_2SO_4 + hexylresorcinol	Fine air bubbles; heat, 0	Bubbles; heat, 0	Bubbles; heat, 0
62	K_2CrO_4	Yellow (A)	0	0
63	$Co(NO_3)_2$	Pink pinholes (A)	Greenish large tables (C)	Changes to purplish brownish pink (C) ?
64	$Cr(NO_3)_2$	0	0	0
65	$CuSO_4$	Specks	Brownish tables	Brownish (C) ?
66	$AlK(SO_4)_2$	0	0	0
67	$MnSO_4$	0	0	0
68	$SnCl_2$	White (A)	White (A)	White (A)
69	$SrCl_2$	0	0	0
70	Uranium acetate	Yellow strings (A)	Yellow granules (A)	Yellow granules (A)
71	KOH + rochelle salts	White (C)	Sparse ppt. tablets (A)	Sparse tablets and bundles (C)

0 = No color or ppt. A = Amorphous ppt. C = Crystalline ppt.

with one drop of the reagent. The development of colors and/or precipitates was followed by a hand lens or under a microscope. In case a positive reaction developed, quantitative tests were made, using 10 millimolar solutions. Since most of the precipitates were white, such reactions are recorded without differentiating between chalky-white, greyish white, yellowish white, brownish white or other shades of "white."

Little information regarding the chemical reactions of benzoylaconine and aconine were found. Accordingly, 10 millimolar solutions were prepared and tested simultaneously with aconitine (Table II). In case positive results were obtained, confirmatory tests were conducted with other dilutions. The 10 millimolar solutions were the most favorable for color tests. Benzoylaconine may be differentiated from aconitine by confirmatory tests with a number of reagents, although no single reaction may be considered as absolutely definitive. In further distinction, aconine may be differentiated from aconitine or benzoylaconine. Only negative reactions were obtained with aconitic acid.

TABLE III.—SENSITIVITY OF TESTS FOR ACONITINE.

No.	Reagent.	Concentration in Millimols. 4.0.	0.4.	0.04.	0.004.	0.0004.	0.00004.
	Taste test	0.02 cc. bitter; saliv., tingling tongues and cheeks	Bitter; tingling	Bitter; tingling, saliv.	Bitter; slight tingling	Bitter; no tingle	No effect
18	Schiebler	Dense white (A)	Slight white (A)*	0	0	0	0
20	Ecolle	Fluffy white (A)	Slight white (A)*	0	0	0	0
24	Wagner	Curdy brown (A)	Lt. brown ppt.*	0	0	0	0
26	Dragendorff	Immed. dense white flocc. (A)	Immed. sparse white flocc. (A)*	0	0	0	0
28	Mayer	Immed. dense white flocc. (A)	Immed. sparse white flocc. (A)	Slowly turbid opalescent, white (A)*	0	0	0
31	$KMnO_4$	Purple (A)	Slight purple (A)*	0	0	0	0
48	Picric acid	Dense yellow (A)	Slight yellow (A)*	0	0	0	0
58	Dimethylglyoxine	White (A)*	0	0	0	0	0
68	$SnCl_2$	Curdy white (A)*	0	0	0	0	0

* Limit of sensitivity. A = Amorphous ppt.

Very little information was found in the literature regarding the sensitivity of various tests for aconitine (9, 14, 16, 18, 23). Those reagents which gave promising results were tested with various dilutions of aconitine, ranging from 4 millimolar down to 0.00004 millimolar (Table III). No positive reactions were obtained with 0.04 millimolar or weaker solutions except Mayer's reagent, which gave a positive reaction at 0.04 millimolar, and thus proved the most sensitive of the reagents studied. The limiting concentrations for the other reagents are reported. No efforts were made to study intermediate concentrations. In making taste tests, 0.02–0.05 cc. of solution was placed upon the tongue: one minute later the mouth was thoroughly rinsed with tap water. Taste phenomena were recorded for fifteen minutes (bitterness, tingling, etc.).

In order to determine the toxicological applicability of these reagents (5, 15, 23), a post-mortem examination was conducted upon a dog which had died following the oral administration of Tincture of Aconite, U. S. P. X. The stomach and contents, the intestine and contents, a portion of muscle of the thigh, the liver, one kidney and the spleen were removed and examined separately. Each tissue was chopped fine and extracted with alcohol containing 1 per cent of tartaric acid.

When extraction was complete, the material was filtered, the alcohol evaporated off on a water-bath at a low temperature, and the residue taken up with water. After standing until solution appeared complete, this was filtered and the solvent evaporated off on a water-bath. This process was repeated with alcohol and water a second time, yielding eventually a residue which was completely soluble in alcohol and water. This was dissolved in 5 cc. of distilled water and tested (Table IV). Since tincture of aconite had been administered to this dog daily over a period of several months, it might be anticipated that distribution in the cadaver would differ from that to be expected following acute poisoning. Positive results were obtained in tests conducted on extracts of the stomach and intestine, indicating that absorption was not complete in the interval of ten hours since the administration of the last dose. Strongly positive results were obtained in testing the liver, but negative results were obtained from the kidney, spleen and the muscles. Following the administration of a single dose of an aconite preparation to dogs, positive reactions have been obtained in extracts of the liver, and doubtful or negative reactions in extracts of the kidneys. It would appear that the aconite alkaloids are excreted largely into the liver.

TABLE IV.—TOXICOLOGICAL TESTS FOR ACONITINE IN VISCERA.

No.	Reagent.	F. E. Aconite.	Stomach.	Intestine.	Liver.	Kidney.	Spleen.	Muscle.
18	Schiebler	White (A)	Brown (A)	Brown (A)	0	0	0	0
20	Ecolle	White (A)	Brown (A)	Brown (A)	Brown (A)	Brown (A)	0	0
24	Wagner	Lt. brown (A)	Lt. brown (A)	Lt. brown (A)	0	0	0	0
26	Dragendorff	Dark brown curdy (A)	Lt. brown curdy (A)	Lt. brown (A)	Flocculent (A)	Flocculent (A)	0	0
28	Mayer	Lt. brown (A)	Lt. brown (A)	Lt. brown (A)	Lt. brown (A)	0	0	0
31	$KMnO_4$	Brown (A)	Brown (A)	Brown; no ppt.	Brown (A)	0	0	0
48	Picric acid	Yellow (A)	Yellow (A)	Yellow (A)	Yellow (A)	0	0	0
58	Dimethylglyoxine	White (A)	Brown (A)	Brown (A)	Brown (A)	0	0	0
68	$SnCl_2$	0	Brown (A)	Brown (A)	Brown (A)	0	0	0

A = Amorphous ppt.

CONCLUSION.

1. The behavior of aconitine, benzoylaconine and aconine have been determined with 71 alkaloidal reagents. Characteristic reactions for the differentiation of these three alkaloids have been developed.

2. Mayer's reagent, which was the most sensitive chemical test for aconitine, had a limiting threshold at a concentration of 0.04 millimolar; the taste test detected tingling at 0.004 millimolar, and bitterness at 0.0004 millimolar concentrations.

3. A substance giving the chemical reactions of aconitine has been detected in the liver, stomach and intestines of dogs, but not in the kidneys, spleen or muscle.

AUTHORS' NOTE: We wish to express our appreciation to Richard I. Grantham and the late Dr. Herman Engelhardt for the benzoylaconine and aconine used in this investigation.

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GAMMA RAYS.

Discovery of a way to make sodium give out gamma rays has been announced by Prof. Ernest O. Lawrence at the University of California on October 20th. The radiation, it is believed, will open a promising field for cancer research and a further study of how radiation acts on living tissues.

DETERIORATION AND STABILIZATION OF ACONITE PREPARATIONS. PART I.[1,2]

BY WILLIAM B. BAKER.

INTRODUCTION.

The reports of early investigators on the value of aconite as a therapeutic agent were more often conflicting than otherwise. It is now believed that this was due primarily to the fact that the drug and its preparations decreased rapidly in potency due to the instability of aconitine, which is the physiologically active principle. The fact that aconitine is not stable has been known for some time, but it was not until comparatively recent times that attempts to measure accurately its rate of deterioration have been made, and likewise to stabilize the preparations of aconite and aconitine.

In their studies of the deterioration of aconite preparations Swanson (1), Squibb Research Laboratories (2) and Swanson and Hargreaves (3), found that these preparations deteriorated rapidly within a year. It was shown that deterioration is due to the hydrolysis of aconitine into benzaconine and aconine, and that deterioration is directly dependent upon the hydrogen-ion concentration of aconite preparations.

With the object in view of determining the rate of deterioration of aconite preparations (this paper covers only the tincture) and of determining which of the stabilizers in use are the most efficient, the following experimental studies were made. Incidentally, the accuracy of the U. S. P. X method of assay was also studied.

EXPERIMENTAL.

Preparation of Samples.—Dried tubers of *Aconitum napellus* were subjected to examination by a botanist and found to be as represented with respect to identity. The drug was reduced to a No. 40 powder by grinding, and two tinctures of aconite were prepared. Tincture No. 1 was prepared in strict accordance with the U. S. P. X procedure for Tincture of Aconite (7). Tincture No. 2 was prepared by the same method, but with the addition of 2 per cent acetic acid to the 70 per cent alcoholic menstruum, a procedure recommended as being the most desirable to insure stability.

The tincture was selected as the preparation for this study as it is the preparation of aconite most frequently used, and because it is typical of the other liquid preparations of aconite in so far as lack of stability is concerned.

Tincture No. 1.—120-cc. portions of this tincture were measured off by a burette into eleven amber-colored bottles of 125 cc. capacity. Before filling, the bottles were immersed for 24 hours in water acidulated with 2 per cent hydrochloric acid, to neutralize any possible alkalinity of the glass, then thoroughly rinsed with water.

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[1] From the laboratories of A. G. Du Mez, Professor of Pharmacy, and M. R. Thompson, Professor of Pharmacology, School of Pharmacy of the University of Maryland. Compiled, in part, from a thesis submitted to the Faculty of the Graduate School of the University of Maryland in partial fulfilment of the requirements for the degree of Master of Science, 1933.

[2] Scientific Section, A. PH. A., Washington meeting, 1934.

Each portion, except one, which was used as a control, was acidified with a definite amount of acid as shown below, and the p_H values determined within a day or two.

TABLE I.—p_H VALUES OF PORTIONS.

Portion.	Per Cent Acid Added.	p_H Value.
1	None	5.7
2	0.1 hydrochloric acid	3.8
3	0.2 hydrochloric acid	2.4
4	0.3 hydrochloric acid	2.3
5	0.4 hydrochloric acid	1.9
6	2.0 acetic acid	4.6
7	2.5 acetic acid	4.5
8	3.0 acetic acid	4.45
9	3.5 acetic acid	4.4
10	4.0 acetic acid	4.3
11	2.0 hypophosphorous acid	1.15

Acetic and hydrochloric acids were used for acidifying as they had been used for this purpose by other investigators.

Hypophosphorous acid was used because of its reducing properties and because it was thought that deterioration might be due, in part at least, to oxidation of the alkaloids. The p_H value obtained for this portion was so low (p_H 1.15) that it appeared as though the amount of hypophosphorous acid added (2 per cent) was more than sufficient to give the value (approximately p_H 2.5–3.0), reported by other investigators as being the most desirable. To determine if this was actually the case, 25 cc. of non-acidified tincture were accurately measured off and adjusted for p_H value by adding successive small amounts of acid measured from a burette. The following results were obtained:

TABLE II.—ADJUSTMENT OF p_H VALUE WITH HYPOPHOSPHOROUS ACID.

Cc. of Hypophosphorous Acid Added.	p_H Value.
0.1	3.0
0.2	2.7
0.3	2.6
0.4	2.0

Tincture No. 2.—One liter of tincture was prepared using a 70 per cent alcoholic menstruum acidulated with 2 per cent acetic acid. The tincture was not divided into portions as in the case of Tincture No. 1, but was preserved in one bulk for observation. The p_H value of this tincture was found to be 4.80.

The addition of the same percentage of an acid will give variable p_H values in preparations made from different lots of drugs, due to the variable amounts of alkaloids and inert extractive matter present. Therefore, it is inadvisable to specify what percentage of acid should be added to the preparation for stabilizing purposes. The p_H value that will give the greatest protection to the preparation should be stated instead.

The results of this study show that the use of acetic acid, or even glacial acetic acid, as stabilizers, is impractical because of the comparatively large quantity which must be added to bring the p_H value down to the desired level. The results presented in the following table demonstrate this clearly:

TABLE III.

Hydrochloric Acid. Amount of Acid Added to 30 Cc. of Tincture.	p_H Value.	Acetic Acid (36%). Amount of Acid Added to 25 Cc. of Tincture.	p_H Value.	Acetic Acid (Glacial). Amount of Acid Added to 30 Cc. of Tincture.	p_H Value.
None	5.48	None	4.8	None	4.77
0.1 cc.	2.97	3.8 cc.	3.7	0.5 cc.	4.33
0.2 cc.	1.74	6.2 cc.	3.4	2.5 cc.	3.85
		7.7 cc.	3.3	4.5 cc.	3.47
		10.0 cc.	3.1	7.0 cc.	3.17
		11.7 cc.	3.0	9.0 cc.	2.98
		13.6 cc.	2.8	11.0 cc.	2.82
		17.5 cc.	2.7	14.0 cc.	2.61
		23.4 cc.	2.5	16.0 cc.	2.53
				17.0 cc.	2.43
Percentage of acid added to obtain p_H value of 1.74 = 0.66.		Percentage of acid added to obtain p_H value of 2.50 = 93.60.		Percentage of acid added to obtain p_H value of 2.43 = 56.66.	

Assay of Samples.—The method used for the assay of Tinctures Nos. 1 and 2 is the one described in the U. S. P. X (7) under Tincture of Aconite. The samples prepared were assayed at intervals of approximately three months.

The portions to be assayed were diluted so that the dose to be administered to the animal would come within a convenient injection range (0.4–1 cc.). Warm tap water, chlorine free, was used for making the dilutions.

TABLE IV.—RATE OF DETERIORATION OF TINCTURE NO. 1.

			Date of Assay.							
Portion.	Acid Used.	p_H.	10–29–31. Per Cent Strength.	1–29–32. Per Cent Strength.	5–2–32. Per Cent Strength.	8–2–32. Per Cent Strength.	11–28–32. Per Cent Strength.	3–12–33. Per Cent Strength.	3–8–34. Per Cent Strength.	p_H.
1	None	5.7	114	66	Below 50	...	...	...	...	5.56
2	HCl	3.8	...	89	80	...	...	Below 50	...	4.40
3	HCl	2.4	...	100	...	89	72	...	...	2.89
4	HCl	2.3	...	114	...	114	...	114	114	2.85
5	HCl	1.9	...	114	...	114	114	100	...	2.36
6	CH_3COOH	4.6	...	100	66	Below 50	...	...	...	4.72
7	CH_3COOH	4.5	...	100	...	...	Below 50	...	...	4.63
8	CH_3COOH	4.45	...	89	80	...	...	...	...	4.56
9	CH_3COOH	4.4	...	100	...	100	Below 50	...	...	4.57
10	CH_3COOH	4.3	...	114	114	114	Destroyed	...	...	...
11	H_3PO_2	1.15	...	114	114	114	80	72	...	1.46

The U. S. P. X (7) gives the minimum lethal dose for Tincture of Aconite as 0.00035 cc. to 0.00045 cc. per Gm. weight of guinea pig. Therefore, a tincture, the minimum lethal dose of which is found to be 0.00040 cc. per Gm. weight of animal, would be considered to be 100 per cent with respect to the U. S. P. standard.

Immediately after preparation, Tinctures Nos. 1 and 2 were assayed and found to have a potency of 114 per cent.

The acid used to acidify the portions of Tincture No. 1 apparently had no effect on the animals, as the minimum lethal dose was found to be the same in all cases, as shown in the table which follows. This table also shows the rate of deterioration as revealed by assays made at intervals, in all but one instance, of approximately three months.

The stabilizing effect of the addition of acid is clearly shown by the foregoing results. Tinctures prepared without the addition of acid deteriorate rapidly. Hydrochloric acid is shown to be the best stabilizer of the acids employed. This is demonstrated particularly well by the assay results for "portion 4" of Tincture No. 1, which had an initial p_H value of 2.30. In this case, hydrochloric acid appears to have afforded complete protection over a period of twenty-nine months. In other portions acidified with hydrochloric acid the protection was not so striking, deterioration increasing with an increase in p_H value.

TABLE V.—RATE OF DETERIORATION OF TINCTURE NO. 2.

	Date of Assay.				
	10–29–31. Per Cent Strength.	1–29–32. Per Cent Strength.	8–2–32. Per Cent Strength.	3–12–33. Per Cent Strength.	
p_H.					p_H.
4.8	114	100	89	72	4.94

Acetic acid proved less efficient than hydrochloric acid. It retarded deterioration to a moderate extent when added in sufficient amount. When acetic acid was added to the menstruum instead of the percolate, as shown by Tincture No. 2, deterioration also took place, although not to the same extent as when the same percentage of acid had been added to the percolate as is the case in "portion 6" of Tincture No. 1.

Hypophosphorous acid, likewise, afforded only moderate protection.

Based on the foregoing results it may, therefore, be said that hydrochloric acid is preferable to acetic acid as a stabilizer for tincture of aconite for the following reasons:

I. It possesses greater ionizing power than acetic acid.

II. Having better ionizing properties, much less hydrochloric acid is necessary for adjusting the preparation to the desired p_H value than when acetic acid is used.

Hydrochloric acid is preferable to hypophosphorous acid as a stabilizer for tincture of aconite because it possesses greater ionizing power and is more economical.

Approximately four months after Tinctures Nos. 1 and 2 had been prepared, two other tinctures were prepared from the same lot of drug. These two tinctures were numbered 3 and 4, respectively.

Tincture No. 3.—This tincture was prepared from the same lot of powdered aconite tubers used in preparing Tinctures Nos. 1 and 2, the only difference being that in this case the drug had been in the powdered condition for four months, whereas in the preceding cases the drug was ground just before the preparation of the tinctures was begun.

Tincture No. 4.—This tincture was prepared from the drug which had been *kept whole*, and powdered at the end of the four-month period.

The two tinctures, prepared as described, were assayed for potency with the following results:

TABLE VI.—RATE OF DETERIORATION OF DRUG.

Tincture.	Strength in Per Cent.	Assay Date.
No. 3	57	2–15–32
No. 4	73	2–15–32

In the case of Tincture No. 3 where the aconite had been kept over a period of four months in the powdered condition before being made into tincture, the drug shows a loss of 57 per cent, or about half of its strength compared with the results obtained in the initial assays of Tinctures Nos. 1 and 2.

In the case of Tincture No. 4 where the aconite had been kept over this period of time in the *whole* condition before being made into tincture, the drug shows a loss of 41 per cent compared to the initial strengths of Tinctures Nos. 1 and 2.

It appears, therefore, that aconite should not be kept in the powdered condition for any lengthy period of time, but that it should be stored in the whole condition and powdered just previous to making up into tincture or other preparation.

Aconitine.—Swanson and Walters (8) assert that the deterioration of aconite preparations cannot be definitely determined until a more satisfactory method of assay has been developed. Swanson (1) feels that the lethal dose method would be satisfactory for testing the therapeutic efficacy of aconite, providing the total alkaloids were determined in terms of a standard aconitine, and a standard method of technique was employed.

With the intention, therefore, of studying the seasonal variation of guinea pigs (their susceptibility to a stable standard substance at different intervals during the year), and of the use of aconitine as the standard, the following work was undertaken:

Crystalline aconitine (Aconitine Potent, Merck) was recrystallized repeatedly from hot alcohol until its toxicity to guinea pigs became constant. This aconitine, used as a standard throughout the work, was recrystallized six times. The crystals were then dried thoroughly, and sealed *in vacuo* in portions of 20–30 mg. to the ampul.

"Aconitine values," using this pure crystalline aconitine, were determined at each interval of assay of the Tinctures Nos. 1 and 2 (approximately three-month intervals). A 1:50,000 dilution of hydro-alcoholic solvent (about 25 per cent alcohol) constituted the working solution for injection.

Healthy, normal guinea pigs were used for the determination of the aconitine values. These animals had been obtained from one source only, and had been acclimated to laboratory surroundings before being used for assay purposes.

The U. S. P. X method of assay as directed under Tincture of Aconite (7) was followed in the determination of the minimum lethal dose as in the case of the tinctures assayed.

TABLE VII.—ACONITINE VALUES. GM. ACONITINE PER GM. WEIGHT OF GUINEA PIG.

10-29-31.	1-29-32.	5-2-32.	8-2-32.	11-28-32.	3-15-33.
0.000000050	0.000000055	0.000000050	0.000000055*	0.000000055	0.000000050

* In obtaining the "aconitine value" on date of "8-2-32," the weight of one of the guinea pigs used was 465 Gm., which is considerably beyond the U. S. P. range. This procedure was made necessary, however, due to a shortage of guinea pigs at that time. Apparently, however, this did not affect the results to any noticeable extent.

The foregoing aconitine values show that no appreciable change in susceptibility of the guinea pigs to the aconitine took place in 15 months. This is explained by the fact that the guinea pigs used were in an absolutely healthy, normal condition and had been obtained from one source only. This, probably, would not be the

case if the condition of the guinea pigs was poor, if the animals had not been acclimated to laboratory surroundings and if they had been obtained from various sources. This matter is receiving further consideration.

CONCLUSIONS.

1. The use of hydrochloric acid as a stabilizer for tincture of aconite is superior to acetic acid, provided the preparation is adjusted to the correct hydrogen-ion concentration.

2. The use of acetic acid as a stabilizer is impractical because of the large amount required to adjust the preparation to the desirable hydrogen-ion concentration.

3. Aconite in the form of the whole crude drug deteriorates rapidly and the powdered drug deteriorates even more rapidly.

4. Tincture of Aconite U. S. P. X, because of its poor keeping qualities, should be adjusted with hydrochloric acid to a hydrogen-ion concentration sufficient to preserve it (approximately, p_H 2.3–3.0).

5. The resistance of guinea pigs to aconite, or aconitine, is consistent provided the weight range specified by the U. S. P. X is strictly adhered to, and further provided that these guinea pigs are in an absolutely healthy, normal condition.

6. The advisability of the use of aconitine as a bioassay standard will receive more extensive consideration in a later report.

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Henry Ford says he has had hunches, but what others call hunches he calls memories of things learned in past lives; "study the past," he says "and you will see that the congresses and the crowds were always arguing irrelevant and unimportant issues while the real revolution was going on quietly in the laboratory."

DRUG EXTRACTION. I. A STUDY OF VARIOUS MENSTRUA FROM THE STANDPOINT OF SWELLING EFFECTS, PENETRATION AND EXTRACTION.

BY WILLIAM J. HUSA AND LOUIS MAGID.

(*Continued from page 901, September Journal.*)

Swelling of Powdered Belladonna Root.—Studies of the swelling of powdered drugs are obviously of importance, since this is the form in which drugs are extracted. Scoville (2) measured the swelling of a ground drug, 5 Gm. of gentian in about a No. 30 powder being placed in a specially graduated 25-cc. cylinder and the volume measured before and after treatment with a liquid, allowing time for settling. The error caused by the buoyant effect of the liquid on the drug particles was recognized by Scoville.

In the present study this method was improved by centrifuging the mixture of drug and solvent, thus overcoming the buoyant effect of the solvent and obtaining a rather complete and sharp separation of liquid and solid. Graduated centrifuge tubes of 15 cc. capacity were used in a large size centrifuge (Size 1, Type SB, operating at 5 amperes, 110 volts, 60 cycles, made by the International Equipment Co.). The centrifuge was run close to maximum speed, which was kept constant throughout the experiments. Except where otherwise specified, 0.50 Gm. of powdered drug and 8.0 cc. of liquid were used in the experiments, these amounts being found to be most practical. The mixtures of powdered drug and liquid were centrifuged for ten minutes which was the time ascertained by trial as necessary for complete packing. In stating the results, the ten minutes of centrifuging is included in the maceration time. The tests were conducted in duplicate, the volume of the powdered drug being read off on the graduated centrifuge tubes.

TABLE XVI.—SWELLING OF BELLADONNA ROOT (IN NO. 40 POWDER) IN VARIOUS MENSTRUA.

Menstrua. Volume of:			Dry.	Time of Maceration in Minutes.							
Glycerin.	Alcohol.	Water.	0.	10.	20.	40.	60.	120.	360.	720.	1440.
0	0	1	100	161	161	152	161	161	166	171	152
0	1	7	100	152	161	161	161	152	152	161	142
0	1	3	100	142	138	138	142	142	138	142	133
0	1	1	100	123	133	123	128	123	114	114	114
0	7	3	100	119	119	109	114	114	109	114	109
0	5	1	100	104	114	109	114	104	104	109	104
0	9	1	100	114	114	114	114	114	104	104	104
0	1	0	100	114	114	114	104	100	104	104	100
1	0	3	100	138	142	142	142	142	142	142	152
1	0	1	100	138	142	142	142	142	142	142	152
4	0	1	100	123	128	138	142	142	142	142	152
1	3	0	100	104	109	109	109	109	109	109	119
1	1	0	100	104	104	104	104	109	114	114	119
4	1	0	100	100	100	114	114	114	119	133	133
65	250	685	100	119	119	119	119	119	123	128	128
100	500	400	100	104	104	100	104	104	104	104	114
75	675	250	100	104	104	100	100	100	109	104	104

Swelling of Belladonna Root in Various Menstrua.—Through a reputable dealer and miller of crude drugs a 125-pound shipment of belladonna root U. S. P.

was obtained as follows: 10 lbs. whole root, 40 lbs. of 40 mesh and 25 lbs. each of 20, 60 and 80 mesh, prepared according to the following specifications: "The above to be prepared by taking 125 pounds of belladonna root, selecting a representative sample of 10 pounds for the whole root and a representative 40-lb. sample to be milled to 40 mesh and three 25-lb. samples to be milled to 20, 60 and 80 mesh, respectively. Each 25-lb. (or 40-lb.) portion is to be milled separately so that each portion will be as nearly alike as possible except for the difference in the milling." It was thought that by use of this 125-pound supply of the drug, all experiments would be strictly comparable. A thorough study of the shipment was made by C. L. Huyck, and it was found that the drug conformed to the U. S. P. requirements.

For concise presentation, the results in the tables which follow represent the average of two determinations, expressed on a percentage basis, the volume of the dry drug being taken as 100.

With alcohol-water mixtures the results indicate that the swelling decreases with increasing alcoholic content. The No. 40 powder reached a maximum swelling in the first ten minutes in the alcohol-water mixtures; the later noticeable fall in percentage swelling may be due to a softening of the drug after prolonged contact with the liquid and subsequent firmer packing by the centrifugal force.

In glycerin-water mixtures, the final swelling was the same regardless of whether the liquids were present in equal amounts, or whether the glycerin or water was in excess; however, the mixture of glycerin 4 vol.—water 1 vol. required a longer time for reaching maximum swelling. In glycerin-alcohol mixtures there was less swelling than in glycerin-water mixtures. In glycerin-alcohol-water mixtures the swelling after 24 hours was greater with the mixtures having the greater proportion of water.

Effect of Fineness of Powder on Swelling.—Using the official menstruum specified by the U. S. P. X for Fluidextract of Belladonna Root, *i. e.*, a mixture of alcohol 5 vol.—water 1 vol., tests were conducted by the centrifuge method on belladonna root in No. 20, 40, 60 and 80 powder.

TABLE XVII.—SWELLING OF BELLADONNA ROOT OF DIFFERENT DEGREES OF FINENESS IN A MIXTURE OF ALCOHOL 5 VOL.—WATER 1 VOL.

Powder No.	Dry.	Time of Maceration in Minutes.							
	0.	10.	20.	40.	60.	120.	360.	720.	1440.
20	100	113	117	113	113	113	130	130	117
40	100	100	104	109	109	104	104	114	104
60	100	100	100	100	100	105	105	105	105
80	100	105	110	115	115	115	115	115	115

The volume occupied by a given weight of powdered drug would naturally be greater for the coarser powders, since large particles pack less efficiently than small particles in a given space. The results in Table XVII indicate that for the No. 20, 40 and 60 powders, the larger the powder, the greater the apparent swelling; this may be due to the fact that as the larger particles swell, the packing becomes still less efficient. An opposing tendency, however, arises in the fact that swelling takes place largely near the surface, so that small particles should show a greater percentage swelling on the basis of this factor taken by itself. In the No. 80 powder, the greater swelling as compared with the No. 40 and 60 powders may be due

to an overbalancing of the factor of efficiency of packing by the factor of the increased coefficient of swelling in smaller particles.

Effect of Proportion of Liquid in Maceration on Swelling.—This point was considered from the standpoint of the effect on percentage swelling in maceration preliminary to packing in a percolator. Tests have been carried out by the centrifuge method, by the use of an oedometer (3), and by a packing method using a graduate.

For tests of swelling of drug powders with small amounts of moistening liquid, a further study of methods is required, since the results obtained by the different techniques are contradictory to a certain extent; however, the results seem to indicate that maximum swelling is not attained with amounts of liquid ordinarily used in moistening drug powders preparatory to packing in a percolator.

Discussion of Results on the Swelling Effect of Solvents.—The drying of a drug represents primarily a removal of water, although other secondary changes occur. Tissues are originally more or less saturated with water, and a marked decrease in size results from drying, due perhaps in greatest measure to loss of turgidity and collapse from loss of water. From these considerations it would be natural to consider swelling as primarily a reversal of the drying process, with some differences due to the irreparable damage to the plant protoplasm during the drying. The hydration of such dried material (4) would take place as in other dead material by means of imbibition and adsorption, with osmosis by the action of vacuolar materials almost eliminated. This illustrates the botanical maxim that when a living cell dies, it loses its osmotic powers.

While water seems to be the natural swelling agent, some other liquids, such as alcohol, resemble water sufficiently to be taken up by the tissues. It would seem that, in order to cause swelling, a liquid must permeate the tissues and wet the inner surfaces. The swelling by absolute alcohol would be an example of this; it is possible that the momentary shrinkage caused by absolute alcohol is due to the abstraction of water from the tissues and that the swelling which follows is due to the gradual permeation of the cells by absolute alcohol. In the tests on swelling of strips of chestnut wood in absolute alcohol it was recognized that there was a possibility that the absolute alcohol on the slide might take up sufficient moisture from the air to affect the results. However, the tests on blocks of chestnut wood were carried out in stoppered and sealed flasks thus eliminating any possible effect of moisture from the air and it was thus established that the swelling effects are due to absolute alcohol itself.

The slower approach to equilibrium in the glycerin-water and alcohol-water mixtures might be thought of as due to a slower permeability of the cells to the alcohol-water and glycerin-water mixtures.

The fact that concentrated glycerin solutions cause only one per cent of swelling may be due to the stability of glycerin hydrates, or to a lack of permeability of the cells to concentrated glycerin solutions. The well-known affinity of glycerin for water is probably due in part to the formation of hydrates. Such water of hydration would not be available for hydration of the dried plant tissues unless these had a greater attraction for the water than the glycerin had, in other words the distribution of water between the tissues and the glycerin would depend upon the composition and relative stability of the respective hydrates. Glycerin caused a shrinkage of the blocks of chestnut wood, followed by recovery and gradual swelling. The results are reminiscent of the observation by Klebs (5) in 1888, that plant cells placed in a solution of glycerin first underwent plasmolysis and then gradually recovered, thus indicating gradual permeation by the glycerin.

Ethylene glycol, diethylene glycol and carbitol cause about the same percentage swelling as does water, except that water comes to equilibrium much more rapidly. Propylene glycol and dioxan caused less swelling than alcohol.

In general the results with the glycerin-water, glycerin-alcohol and alcohol-water mixtures indicate that the swelling in mixtures of two liquids is practically an average of the effect of the liquids themselves when allowance is made for the relative proportions of the two liquids in the mixture. An examination of the graphs (see Graphs 1 and 2) indicates that the general form

of the swelling curves is very similar for alcohol-water and glycerin-water mixtures. However, there are some noteworthy differences, in that a smaller proportion of glycerin than of alcohol is required to bring about a decrease in the primary swelling and a lengthening of the period necessary for the attainment of equilibrium, and in that the addition of one part of water to 9 parts of glycerin has no effect on the swelling curve, but in the corresponding alcohol-water mixture there is a difference.

The results of the work on strips of chestnut wood indicated that a variation in p_H in aqueous solutions had no effect on the swelling, but in the work on blocks of chestnut wood it was found that 0.01*N* aqueous HCl and NaOH both slightly increased the swelling. In alcohol, swelling of woody tissues is decreased by acids, noticeably in 0.1*N* concentration. Alcoholic NaOH decreased the swelling of blocks of chestnut wood, while in the work with strips of chestnut wood alcoholic NaOH increased the swelling. The swelling with strips may be due to a weakening action of the NaOH on the thin sections used. MacDougal (4) also found that tissues swelled more in alkaline solutions; he states further that "acids decrease the hydration capacity of agar and of the pentosans which enter into the composition of certain types of plant cells." The effects of acid and alkali in alcoholic solution are noticeable particularly in cases where the alkali or acid are present in the alcohol when it is first added to the dry wood. If the wood has already been acted upon by the alcohol before the addition of alcoholic acid or alkali, the effect is less noticeable. After a tissue has been treated with alcoholic acid or alkali, treatment with alcohol is able to reverse the effect of the acid or alkali only partially. This result is in accord with the statement of MacDougal (4) that "no swelling agent yet tested has been found to reverse the action of another solution so fully as to bring the dimensions of the sections down to the dimensions which might have been attained in the second agent alone." However, the results obtained on successive additions of solvents show that water, alcohol and absolute alcohol each have a characteristic effect on the tissues and that this individual effect tends to assert itself regardless of whether the solvent is applied to a dried tissue or to one that has already been treated with another solvent.

Comparative Swelling with Grain and across Grain.—Current theories regarding the structure of the cell wall offer an explanation for the fact that swelling of wood is greater across the grain than with the grain. In 1858, Nägeli (6) proposed a theory that the cell wall consists of ultramicroscopic, crystalline, molecular complexes, which he called micellæ, and which were supposed to be arranged spirally. Likewise, in 1924 Koehler (7) stated that theoretically the cell walls are made up of ultramicroscopic fibrils running spirally in the cell walls, the water being held almost entirely between the fibrils. According to Schorger (8) each micella is normally surrounded by a film of water, but in the dry condition the micellæ are drawn together. On exposure to water, "swelling takes place up to the point where the pressure of the aqueous layers equals the cohesion between the micellæ."

On the basis of X-ray investigations, Sponsler (9) concluded that the structural units of the cell walls of fibres are $C_6H_{10}O_5$ molecules attached in chains running parallel to one another and very uniformly spaced. According to Sponsler and Dore (10) the $C_6H_{10}O_5$ molecules themselves are held together to form chains by bonds of primary valence, while the chains are associated and held together by bonds of secondary valence. They state that since the $C_6H_{10}O_5$ molecules are held together by primary valence, water molecules cannot penetrate between them and consequently longitudinal swelling of cellulose fibres cannot occur to any great extent. The swelling across grain is explained on the basis that water is able to penetrate between the chains, which are held together by secondary valence only. The water molecules become adsorbed upon the oxygen atoms, thus increasing the distance between the parallel chains and causing swelling.

Swelling of Fresh and Dried Woody Tissues.—There is practically no swelling of the fresh blocks of oak sapwood and of Elberta peach wood in liquids. However, the fresh oak sapwood absorbed 12 per cent of its weight of water and the fresh Elberta peach wood absorbed 42 per cent of its weight of water during the time of the experiment. This situation is explained on the basis that the liquids which enter open spaces in the wood do not cause swelling but merely occupy space which was previously filled with air. Thus Hawley and Wise (11) have stated that the water held in the microscopic cell cavities does not cause swelling of wood. According to Detmer (12) the mere filling of the lumina of the wood elements with water cannot bring about

any increase in volume of the material, but only the liquid imbibed by the solid substance causes swelling. Detmer states that imbibition is by no means capillarity; a fluid entering by capillarity occupies previously existing spaces, while when imbibition takes place, the molecules of the liquid push in between the micelles actually making space for themselves and thus bringing about an increase in volume. These considerations make clear how a liquid may be absorbed in quantity in the open spaces in the plant tissues and yet may not cause appreciable swelling either because the micelles are already distended as in fresh wood or because the liquid does not have the properties facilitating imbibition as distinguished from capillarity. Steel (13) takes the view that when a substance absorbs a liquid without swelling, the cohesion of the molecules of the substance is too great to permit them to be forced apart by the liquid.

In studying the data concerning the effect of water and other liquids on blocks of woody tissues dried to constant weight, we find that recovery of original size occurs to a greater extent and at a more rapid rate with the blocks dried at room temperature than with the ones dried in an oven at 90° C. These results are in accord with the general rule of colloid chemistry that gels which have been partially dehydrated have a lowered capacity for reimbibing water. This has sometimes been explained on the basis that during drying the salts and other dissolved substances are finally left in a concentrated form on the tissue surfaces, and thus affect imbibition in a different manner than when diffused in dilute form.

Effect of Thickness of Woody Tissue on Swelling.—MacDougal (4) showed that in thin sections, the coefficient of expansion is relatively high and solvation is attained quickly. Our results are in agreement; thus the chestnut wood blocks increased only 7 per cent in thickness while the thin sections (0.05 mm.) increased 20 per cent in width. Cells at or near the surface of a section or block may swell until the forces causing swelling are counter-balanced by the elastic force of the stretched cell wall. Cells on the interior of a block, in order to swell, must overcome not only the elastic forces of their own cell walls but also the restrictions of the surrounding cells; in blocks possessing considerable rigidity it can be readily understood that the inner cells must swell less than the outer cells and thus the coefficient of expansion is relatively low in thick pieces or blocks. In a block the outer layers would cause the greater amount of swelling. This is in accord with our results, which show that the greater part of the swelling of blocks took place in considerably shorter time than was necessary for the liquids to penetrate to the center of the blocks. (*To be continued.*)

STUDIES ON STRYCHNINE. III. THE EFFECTIVENESS OF SUCROSE, SACCHARIN AND DULCIN IN MASKING THE BITTERNESS OF STRYCHNINE.*[1]

BY JUSTUS C. WARD, JAMES C. MUNCH,[2] H. J. SPENCER AND F. E. GARLOUGH.

Earlier papers in this series (1, 2) on the masking of the bitter taste of strychnine gave the results of experiments with a number of chemically unrelated substances. The results obtained with 1.5 and 10 per cent sucrose solutions suggested the desirability of continuing and extending studies with sucrose as well as with other sweetening agents.

In the series of tests reported in this communication, strychnine alkaloid, sulphate and hydrochloride were obtained from several manufacturers. Chemical tests showed the purity of the products used. The sucrose was a sample of factory-run beet sugar. Soluble saccharin and *p*-phenetylurea (dulcin) were obtained from commercial sources. The technic used in our previous studies was followed here. Five cc. of a solution of strychnine and 5 cc. of a solution of the sweetening agent

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* Scientific Section, Miami meeting, 1931.

[1] Bureau of Biological Survey, U. S. Department of Agriculture.

[2] Sharp and Dohme, Glen Olden, Penna.

were mixed. The mixture was retained in the mouth for exactly one minute and then ejected. Two principal observations were made: (1) the instant at which the bitter taste was first perceptible, and (2) the effect of the bitterness on the strength of the sweet taste. Two individuals (W and S) were consistently available, so most of the figures presented are averages of the results obtained by them. The other investigators made similar studies, but not in such detail. Their results are in substantial agreement. A considerable period of time was allowed to elapse between taste tests to avoid the possible potentiation of strychnine taste. In a series of studies on this point we have found that an interval of fifteen to thirty minutes between tastes is desirable.

The threshold taste limens of the sweetening agents and of the strychnine compounds were first determined. The concentration of the sweetening agent was then increased to 10, 20, 30, 40, 50, 60, 80 and 100 times its threshold, and the limen for the strychnine compound determined at each sweetness concentration. The experiments to determine the efficiency of each of the three sweetening agents in masking bitter taste were conducted as separate tests. The thresholds for the unmixed solutions are given in Table I. The values for the strychnine products are in substantial agreement with the average values obtained upon five individuals in the previous tests, and on forty students tested at Temple University during the last two years.

TABLE I.—THRESHOLD TASTE LIMENS OF HUMAN BEINGS.

Product.	Threshold Concentration. Millimols/Liter.	Gamma/5 Cc.
Sucrose	22.20	38,000
Saccharin	0.067	80
Dulcin	0.10	90
Strychnine as:		
Alkaloid	0.00347	5.8
Sulphate	0.00323	5.4
Hydrochloride	0.00323	5.4

TABLE II.—TASTE LIMENS FOR SUCROSE-STRYCHNINE TESTS.

Concentrations as millimols/liter.

Sucrose.	Strychnine in the Form of: Alkaloid.	Sulphate.	Hydrochloride.
0	0.00347	0.00323	0.00323
22	0.00333	0.00333	0.00323
222	0.00363	0.00348	0.00363
444	0.00572	0.00500	.....
667	0.00800	0.00616	0.00667
890	0.01142	0.01142	.....
1110	0.02000	0.02000	0.01820
1330	0.03330	0.02500	.....
1785	0.03330	0.03640	0.03640
2220	0.05000	0.05720	0.04440

The relative sweetness of saccharin and of dulcin in terms of sucrose has been studied by previous investigators, and divergent conclusions reached because of the variations in concentrations used as "isodulceous" standards. Saccharin has been reported to be 200 to 700 times as sweet as sucrose (3) and the threshold concentra-

tions reported to be 10 mg. per liter. This would correspond to 50 gamma of saccharin in the 5-cc. portion tasted in our technic. We find the absolute quantity of saccharin detectable under our conditions to be 80 gamma. The threshold taste concentrations for sucrose reported in the literature vary from 5 mg. to 60 mg. in 5 cc., although the absolute quantities claimed to have been detected are 3 gamma and 58 gamma. In our experiments 38 mg. (38,000 gamma) proved to be the limiting quantity. This would mean that saccharin is 38,000/80 or 475 times as sweet as sucrose under our testing conditions.

Similarly, dulcin has been reported to be 70 to 350 times as sweet as sucrose, according to the sucrose concentration with which it was compared. In our tests the threshold was 90 gamma, or it was 38,000/90 or 420 times as sweet as sucrose. It is probable that the sample of dulcin used in these tests was purer than the samples used by other investigators.

The detailed findings of the taste limens for strychnine in the form of the alkaloid, the sulphate and the hydrochloride in sucrose solutions are given in Table II. The first line shows the concentration in millimols per liter in aqueous solution which just produced the characteristic strychnine bitterness taste. The succeeding figures show the thresholds with increasing concentrations of sucrose. A sucrose solution, ten times its threshold concentration, had only a slight masking action. A concentration twenty times the threshold shows a beginning protection, which increases rather irregularly with further increase in sucrose concentration. The highest concentrations of sucrose studied appeared to give somewhat greater masking effects on the strychnine sulphate solution than on the alkaloid and somewhat less on the hydrochloride. It is not felt, however, that these differences are necessarily significant. The solution of sucrose 100 times its threshold masked 14 to 18 times the threshold of strychnine and its salts.

TABLE III.—TASTE LIMENS FOR SACCHARIN-STRYCHNINE TESTS.

Concentrations as millimols/liter.

Saccharin.	Strychnine in the Form of: Alkaloid.	Sulphate.	Hydrochloride.
0	0.00347	0.00323	0.00323
0.067	0.00333	0.00363	0.00351
0.667	0.00363	0.00400	0.00400
1.333	0.00400	0.00470	.....
2.000	0.00444	0.00616	0.00533
2.67	0.00500	0.00667	.....
3.33	0.00533	0.00800	0.00800
4.00	0.00572	0.01000	.....
5.33	0.00667	0.01600	0.01000
6.67	0.00800	0.02220	0.01600

The detailed findings of the taste limens for strychnine and its salts in saccharin solutions are given in Table III. Increasing concentrations of saccharin again proved effective in masking the bitterness of strychnine. A marked difference was found, however, in tests upon the alkaloid and upon the salts. The 100-fold saccharin solution masked somewhat more than two times the threshold of the alkaloid, but five times the concentration of strychnine as the hydrochloride and seven times the threshold as the sulphate. Our previous studies have shown the

"common ion effect" produced by sodium salts (2), although we did not obtain as great an effect as this. It is also conceivable that these strong solutions through influences on the osmotic pressure may influence the rates of absorption.

Because of the limited solubility of dulcin, it was not possible to obtain so extensive a series of solutions. The detailed data are given in Table IV. In general, dulcin tends to resemble saccharin; that is, there is an increased masking effect with an increase in dulcin concentration, and the masking action is about twice as great against the salts as against the alkaloid. The strongest solution tested, which was twenty times the threshold for dulcin, protected against somewhat less than two times the threshold for the alkaloid and against somewhat more than three times the threshold for strychnine as the sulphate or hydrochloride.

TABLE IV.—TASTE LIMENS FOR DULCIN-STRYCHNINE TESTS.

Concentrations as millimols/liter.

Dulcin.	Strychnine in the Form of: Alkaloid.	Sulphate.	Hydrochloride.
0	0.00347	0.00323	0.00323
0.10	0.00333	0.00348	0.00348
1.00	0.00363	0.00421	0.00470
2.00	0.00572	0.01000	0.01000

TABLE V.—MASKING POWER OF SWEETENING AGENTS AGAINST STRYCHNINE.

Gm. required to mask 1 Gm. of strychnine.

Threshold Concentration of Strychnine.	Saccharin. Strychnine as: Alkaloid.	Sulphate.	Dulcin. Strychnine as: Alkaloid.	Sulphate.	Sucrose. Strychnine as: Alkaloid.	Sulphate.
1	14.3	13.2	16.1	15.5	6,790	6,790
10	131	120	147.5	128.5	62,350	63,400
20	240	204	188	188	79,100	90,500
30	326	234	...	...	74,000	110,050
40	382	260	...	...	79,600	79,500
50	452	260	...	...	57,000	57,000
60	502	288	...	...	40,700	54,400
80	578	240	...	...	54,350	50,000
100	522	216	...	...	45,500	39,800

For the practical application of these results, Table V has been prepared to show the number of grams of each sweetening agent required to mask the bitter taste of one Gm. of strychnine as alkaloid or as sulphate in various multiples of the threshold bitter taste. For example, the threshold concentration of strychnine having a bitter taste is 5.8 gamma per 5 cc., or 1.16 mg. per liter. If 1 Gm. of strychnine is dissolved in 862 liters of water to give a concentration of 1.16 mg. per liter (the threshold concentration recorded in Table V) it would be necessary to dissolve in this solution 14.3 Gm. of saccharin, 16.1 Gm. of dulcin or 6790 Gm. of sucrose to mask its bitter taste. As the concentration of strychnine is increased, the sweetening agents become relatively more effective. Saccharin appears to be the most efficient of these sweetening agents, but tremendous amounts are required for masking purposes.

As the concentration of strychnine in a sweetening agent was increased, loss in sweetness developed before any bitter taste could be detected. This was particularly noticed with strong concentrations. When solutions of sucrose fifty times the

threshold, or stronger, were mixed with strychnine in any form, marked nausea was noted by one of us. This was observed even though the solution was almost tasteless from neutralization of the sweet and bitter tastes. When strychnine in any form was mixed with solutions of saccharin or of dulcin at concentrations fifty times their sweetness threshold or above, a peculiar metallic flavor resembling dental amalgam was observed.

Variation of individuals in speed of bitterness perception was again confirmed. One of us was able to identify the bitter taste of strychnine at a given concentration in two to ten seconds, another required fifteen to twenty seconds. The opposite condition prevailed for detecting sweet tastes, the "bitter-slow" being "sweet-fast." These differences in rate of apperception were not associated with any marked variation in absolute threshold taste limen, which is in accord with our previous findings (2).

CONCLUSIONS.

1. Sucrose, saccharin and dulcin mask the bitter taste of strychnine as the alkaloid, sulphate or hydrochloride.

2. Sucrose masks the bitterness of the alkaloid and the salts to about the same extent, a concentration one hundred times its sweetness threshold masking fourteen to eighteen times the strychnine threshold.

3. A solution of saccharin one hundred times its threshold masks somewhat more than two times the threshold of the alkaloid, and five to seven times the thresholds of the salts.

4. A solution of dulcin twenty times its threshold masks somewhat less than two times the threshold of strychnine alkaloid, and somewhat more than three times the thresholds of the salts.

5. Increasing concentrations of sweetening agents increased their masking effects.

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PHARMACOLOGICAL AND CHEMICAL STUDIES OF THE DIGITALIS GROUP. I. ADONIS, APOCYNUM AND CONVALLARIA.*

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Although a very large number of papers have been published dealing with various phases of studies conducted upon digitalis, no systematized and concerted investigation of the pharmacology and chemistry of other members of the digitalis

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* Preliminary reports at Miami meeting, 1931, and Washington meeting, 1934.

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(Foot-note: We wish to express our appreciation of the assistance rendered by Arnold Quici, Sharp and Dohme, in making many of the bioassays in this study, and to Mrs. Margarethe Oakley, Maryland Department of Health, for assistance in the chemical assays.)

group has been found in the literature. In this investigation, studies were collaboratively conducted upon adonis, apocynum and convallaria. The control products used for these studies were prepared from crude drugs identified by competent pharmacognosists. The bioassay records of two drug manufacturers over a period of some twenty years have been consulted to ascertain the variations in potency of these crude drugs, as offered in commerce. It should be appreciated that these examinations were made voluntarily, before the bioassay requirements of the U. S. P. or N. F. were made effective. In some instances tests were made upon the crude drug only: other samples were reassayed from time to time, to obtain some information on rates of deterioration. Samples of the finished products marketed as tinctures or fluidextracts by various manufacturers were collected and tested. Since no official standards have been prescribed for these products, it was thought of interest to determine the variation in potency of marketed products. It appears that at least some of the drug manufacturers have been voluntarily assaying and standardizing these preparations, even in the absence of official potency requirements. In addition, a detailed search of the literature has been made to learn the potency of such products as reported, even though the authenticity of the test product is not known. In this communication, our results are presented upon adonis, apocynum and convallaria, and certain active principles obtained from these drugs.

Clinical reports state that adonis, apocynum and convallaria resemble digitalis in many particulars in their effects upon the heart. Prescription surveys show that prescriptions are still being written for these products, although their use in the United States is much smaller than is the use of digitalis. Adonis has obtained a definite vogue in Russia, not only as a drug for exerting certain effects upon the heart, but also as a diuretic (4, 5, 9, 10, 15, 16, 17, 18, 22, 25, 29, 30, 32). A glucoside, adonidin, was extracted from adonis and clinical reports have suggested its value. Mercier and Mercier (25), in a detailed study of adonis, separated two glucosides, (1) adonidoside, which is water soluble, and (2) adonivernoside, which is insoluble in water, but soluble in chloroform. Adonidoside was found to be more cardiotropic and myotropic, having only a feeble action on the central nervous system; adonivernoside was a marked diuretic.

Over a hundred years ago it was reported that apocynum was an emetic, cathartic, diaphoretic and diuretic. Pharmacological and clinical studies showed that it had a specific effect upon the heart, resembling that of digitalis and that a glucoside, cymarin, extracted from apocynum had a similar activity. Because of its action as a diuretic, it has been called the "vegetable trocar" (30, 32). Some information in the literature suggested that there were differences in the activity of different species of apocynum. We have made tests on a number of samples of *Apocynum cannabinum* and of *Apocynum androsæmifolium* which were identified, root by root, by Professor William J. Stoneback for us. We found that fluidextracts prepared from each species showed precisely the same physiological activity. If cymarin is the active principle, as has been suggested, this would be expected in view of Cushny's report (5) that cymarin is identical whether extracted from *A. cannabinum*, *A. androsæmifolium* and *A. venetum*.

Studies on convallaria have shown that the flowers are richer in active principles than are the roots. Karrer (21) in a series of chemical studies supplementing

the earlier investigations of convallaria, (11, 16, 18, 20, 23, 24, 35) has obtained a crystalline glucoside, convallatoxin, which is somewhat less than twice as toxic for frogs as is ouabain.

Review of the literature on adonis showed that tests have been made upon frogs, guinea pigs, rabbits and cats; in Table I results reported in the original articles have been recalculated in terms of milligrams of crude drug or of active principle per kilo of body weight of animal. This permits immediate comparison of the potency of any extractive in terms of the crude drug. The bioassays which we have made are recorded in Table II. Studies of deterioration have been rather limited: results obtained in our one-hour frog study and in the study by the cat method reported in the literature are given in Table III. The chemical assay of the sample of fluidextract of adonis tested by the one-hour frog method in Table III was made by a modification of the Knudson-Dresbach method (1, 26). It was found chemically to be 104 per cent of the (chemical) potency of a standard digitalis product simultaneously assayed by the one-hour frog method and found to be in harmony with the U. S. P. X potency requirement. This result is in good agreement with that obtained by the one-hour frog method which showed the product to be 600/550, or 109 per cent of the requirement of the U. S. P. X for digitalis. It is suggested that, if adonis and its preparations are recognized in the forthcoming revision of the National Formulary, the one-hour frog method should be recommended for bioassay, and that the same potency requirement be established for adonis and its preparations as for digitalis and the corresponding digitalis preparations. In other words, adonis, by bioassay, has the same activity as digitalis.

Physiological potencies of apocynum preparations found in the literature are recalculated in terms of milligrams per kilo and given in Table IV. Holste (18) found by perfusion of the isolated frog heart that 0.24 mg. of cymarin was equivalent to 1 mg. of ouabain: other reports in the literature, using the same technique (26) give values of 0.85, 3.54 and 5.38 mg. of cymarin as equivalent to 1 mg. of ouabain. The purity of the cymarin used is unknown. In testing tincture of apocynum by the pigeon emesis method, Hanzlik (13) found that a dose equivalent to 9 mg. of crude drug per kilo produced emesis and 20 mg. per kilo produced death. Baljet's studies (1) by the Gottlieb thirty-minute frog method (26) showed that the M. S. D. of cymarin was 0.12 mg. per kilo, and of ouabain 0.03 mg. per kilo. Two fluidextracts of apocynum were assayed simultaneously by the one-hour frog and the M. L. D. cat method. For Sample A, the M. S. D. was 320 mg. per kilo, the M. L. D. cat value 55 mg. per kilo. For Sample B, the M. S. D. frog value was 280 mg. per kilo, the M. L. D. cat value, 23 mg. per kilo. Our results in assaying fluidextract of apocynum by the frog and guinea pig methods are given in Table V. The fluidextracts to which letters were arbitrarily signed are products purchased on the open market, and these fluidextracts A and B are not those just referred to. Three fluidextracts were reassayed by the frog and guinea pig methods from time to time over 172 weeks to follow any deterioration. One sample by both methods of assay showed an apparent increase in potency, but reassays were not made on these samples subsequently to learn whether these changes were apparent or real. The loss by the guinea pig method appeared to be greater than by the one-hour frog method which showed comparatively little change. The chemical assay showed this fluidextract to be 111 per cent of the potency of a similar digitalis

product, although the bioassays showed this product to be approximately twice the potency of the digitalis product. It is suggested that, if apocynum and its preparations are recognized in the forthcoming revision in the National Formulary no difference be made between various species, and that the one-hour frog method should be recommended for bioassay, and that the potency requirement established for apocynum and its preparations require them to have twice the strength of digitalis and the corresponding digitalis preparations. In other words, apocynum, by bioassay, should have twice the activity of digitalis.

Reports in the literature regarding the physiological potency of convallaria preparations are given in Table VII. Our studies on fluidextracts, are given in Table VIII and on deterioration in Table IX. The four samples studied by the one-hour frog method showed comparatively little deterioration over a period up to 153 weeks. Chemical assays of a fluidextract which was somewhat more than 300 per cent of the U. S. P. requirement for digitalis by the one-hour frog method showed only 70 per cent of the estimated potency. It is suggested that, if convallaria and its preparations are recognized in the forthcoming edition of the National Formulary, the one-hour frog method should be recommended for bioassay and the convallaria products should be three times as potent as the corresponding digitalis preparations. In other words, convallaria, by bioassay, should be three times as powerful as digitalis.

For ready reference, results of the bioassay and chemical assay, as well as the p_H of samples tested by the Wilson hydrogen electrode method are given in Table X.

TABLES.

TABLE I.—REPORTED PHYSIOLOGICAL POTENCY OF ADONIS PREPARATIONS.

All data recalculated to mg./Kg.

		Method of Assay.				
		Frog.		Guinea Pig	Rabbit	Cat
Ref.	Product.	M. S. D. 1 Hr.	M. L. D.	M. L. D. Subcu.	M. L. D. I. V.	M. L. D. I. V.
8	Fluidextract	400	....	..	..	...
17	Fluidextract	450	....	..	..	...
29	Fluidextract	360–430	....	600	..	...
2	Fluidextract	460	3600	..	..	...
31	Fluidextract	450	....	..	..	...
7	Fluidextract	...	....	..	..	100
15	Fluidextract	...	....	..	..	100–140
8	Adonidin	4	....	..	..	...
4	Adonidin	...	3	..	1	...
10	Adonidin	...	38	..	4.6	...
7	Adonidin	...	....	..	..	4.34
14	Adonidin	...	....	..	..	3.0
16	Adonidoside	...	3	..	2.5	...
9	Adonidoside	...	2.5	..	..	0.7
25	Adonidoside	...	2.5	3.5	1.0	...
22	Adonidoside	...	3.3	..	..	4.7
16	Adonivernoside	...	3.7	..	2.0	...
9	Adonivernoside	...	5.9	..	..	1.3
25	Adonivernoside	...	6.0	6.0	2.0	2.2
22	Adonivernoside	...	4.5	..	0.19	2.3

TABLE II.—BIOASSAYS OF ADONIS PREPARATIONS.

All data recalculated to mg./Kg.

Product.	Sample Number.	Frog M. S. D. 1 Hr.	Guinea Pig M. L. D. Subcu.
Crude drug	1	420	480
Fluidextract	2	625	800
Fluidextract	3	610	...
Adonidin	4	5	5.4

TABLE III.—DETERIORATION OF ADONIS PREPARATIONS.

All data recalculated to mg./Kg.

Assay Method.	Original Potency.	Reassay. Age Wks.	Reassay. Potency.	Loss in Activity Per Cent.
M. S. D. 1-hr. frog	420	166	550	24
M. L. D. Cat*	57	36	88	35
M. L. D. Cat*	188	36	262	28

* Product stored was tincture in 70 per cent alcohol (15).

TABLE IV.—REPORTED PHYSIOLOGICAL POTENCY OF APOCYNUM PREPARATIONS.

All data recalculated to mg./Kg.

Ref.	Product.	Method of Assay. Frog. M. S. D. 1 Hr.	Frog. M. L. D.	Guinea Pig M. L. D. Subcu.	Rabbit M. L. D. I. V.	Cat M. L. D. I. V.
8	Fluidextract	120	..	...	...	....
27	Fluidextract	...	..	240	..	....
12	Fluidextract	...	..	300	...	....
7	Fluidextract	...	..	...	...	66
13	Fluidextract	...	..	...	...	70
20	Cymarin	...	..	...	...	0.1
26	Cymarin	...	0.7	...	...	0.125
32	Cymarin	...	0.8*	...	...	....
			2.0[1]			
21	Cymarin	...	0.67	...	...	....

* *Rana temporaria.*

[1] *Rana esculenta.*

TABLE V.—BIOASSAYS OF APOCYNUM PREPRATIONS.

All data recalculated to mg./Kg.

Product.	Sample Number.	Frog M. S. D. 1 hr.	Guinea Pig M. L. D. Subcu.
Fluidextract	1	320	...
Fluidextract	2	280	...
Fluidextract	3	...	160
Fluidextract	4	...	220
Fluidextract	3	...	240
Fluidextract	6	...	400
Fluidextract	7	...	340
Fluidextract	8	320	...
Fluidextract	9	390	...
Fluidextract	10	...	260
Fluidextract	11	250	180
Fluidextract	12	250	180

Fluidextract	13	280	250
Fluidextract	14	220	200
Fluidextract	15	...	250
Fluidextract	A	...	240
Fluidextract	B	...	320
Fluidextract	C	280	180
Fluidextract	D	250	200
Fluidextract	E	280	190

TABLE VI.—DETERIORATION OF APOCYNUM PREPARATIONS.

All data recalculated to mg./Kg.

Assay Method.	Original Potency.	Reassay. Age Weeks.	Reassay. Potency.	Loss in Activity Per Cent.
1-hour frog	250	156	280	11
		172	260	4
1-hour frog	280	16	220	(27)
1-hour frog	220	16	230	4
M. L. D. Guinea Pig	160	76	480	67
M. L. D. Guinea Pig	220	4	180	(22)
M. L. D. Guinea Pig	240	106	400	40
		108	430	30

TABLE VII.—REPORTED PHYSIOLOGICAL POTENCY OF CONVALLARIA PREPARATIONS.

All data recalculated to mg./Kg.

Ref.	Product.	Method of Assay. Frog. M. S. D. 1 Hr.	Frog. M. L. D.	Guinea Pig M. L. D. Subcu.	Rabbit M. L. D. I. V.	Cat M. L. D. I. V.
11	F. E. Root	...	167	...	...	...
35	F. E. Root	...	200–250	...	...	...
28	F. E. Root	...	30*	60	...	...
			50–90[1]			
3	F. E. Root	...	40–70	...	30–70	...
19	F. E. Root	...	250	...	...	...
34	F. E. Root	...	210	...	...	...
8	F. E. Root	200	...	...	...	...
27	F. E. Root	...	...	300	...	...
12	F. E. Root	...	...	300	...	2–
26	F. E. Root	...	...	...	...	50
11	F. E. Herb	...	107	...	...	...
21	F. E. Herb	...	100	...	...	...
35	F. E. Herb	...	150–330	...	...	...
19	F. E. Herb	110–220	100–240	...	...	...
8	F. E. Herb	187	...	...	...	...
11	F. E. Flowers	...	80	...	...	...
11	F. E. Flowers (Freshly dried)	...	50	...	...	...
11	F. E. Flowers (5 yrs. old)	...	90	...	...	...
21	F. E. Flowers	...	55	...	...	...
35	F. E. Flowers	...	100	...	...	...
19	F. E. Flowers	...	90	...	...	...
8	F. E. Flowers	75	...	...	...	...

TABLE VII.—*Continued.*

21	Convallamarin	...	10	...	...	...
35	Convallamarin	...	15	...	...	...
23	Convallamarin	0.3–0.6	...	...	...	...
8	Convallamarin	4.5	...	...	...	...
6	Convallamarin	4.75	...	...	...	...
24	Convallamarin	...	...	...	3–4	...
7	Convallamarin	...	...	...	...	1.68
21	Convallatoxin	...	0.33	...	...	...

* *Rana temporaria.*

[1] *Rana esculenta.*

TABLE VIII.—BIOASSAYS OF CONVALLARIA PREPARATIONS.

All data recalculated to mg./Kg.

Product.	Sample Number.	Frog. M. S. D. 1 Hr.	Guinea Pig M. L. D. Subcu.
Fluidextract	1	...	140
Fluidextract	2	220	...
Fluidextract	3	200	...
Fluidextract	4	200	...
Fluidextract	5	...	300
Fluidextract	6	...	280
Fluidextract	7	...	300
Fluidextract	8	...	320
Fluidextract	9	...	240
Fluidextract	10	...	120
Fluidextract	11	...	160
Fluidextract	12	110	...
Fluidextract	13	150	...
Fluidextract	14	...	180
Fluidextract	15	180	...
Fluidextract	16	150	100
Fluidextract	17	140	100
Fluidextract	18	180	80
Fluidextract	19	170	...
Fluidextract	20	250	260
Fluidextract	21	200	120
Fluidextract	22	195	...
Fluidextract	A	167	160
Fluidextract	B	125	80

TABLE IX.—DETERIORATION OF CONVALLARIA PREPARATIONS.

All data recalculated to mg./Kg.

		Reassay.		
Assay Method.	Original Potency.	Age Wks.	Potency.	Loss in Activity Per Cent.
1-hour frog	175	136	190	9
		152	180	3
1-hour frog	180	1	175	(3)
		137	175	(3)
		153	220	18
1-hour frog	170	28	200	15
		36	200	15
1-hour frog	200	72	170	(18)
		100	200	0
		116	220	9

TABLE X.—COMPARISON OF PHARMACOLOGICAL AND CHEMICAL ASSAYS.

Product.	Potency as Per Cent U. S. P. Tr. Digitalis. 1-Hour Frog.	Chemical.	P_H.
Standard Tr. Digitalis	100	100	..
Tr. Adonis	109	104	5.99
Tr. Apocynum	230	111	5.13
Tr. Convallaria	300	70	5.96
Ouabain:			
53 gamma/cc.	65	81	..
82 gamma/cc.	100	125	..

CONCLUSIONS.

1. Adonis and its preparations bioassayed by the one-hour frog method should have the same potency as digitalis and the corresponding digitalis preparations.

2. Apocynum should have twice the potency of digitalis by the one-hour frog method of assay.

3. Convallaria should be three times as potent as digitalis by the one-hour frog method of assay.

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SOME CONSIDERATIONS OF SILVER PICRATE.*

BY JOHN C. BIRD AND ALFRED BAROL.

This presentation is intended to cover some of the outstanding points evolved during recent work with silver picrate, certain particular merits of which would seem to have hitherto been overlooked. It is hoped that some of the promising results reported here will act as a stimulus to further clinical investigation of this product.

A survey of the literature covering the last 100 years is disappointing in the scarcity of data concerning silver picrate. The compound was first produced as a by-product by Chevreul, in 1809, during his work on indigo and later by Liebig in 1828, who named it "silver carbazotate," and noted its explosive property. To Dumas (1) however, might be ascribed the credit of first preparing silver picrate, as such, from silver nitrate and ammonium picrate, in 1841. Dumas published an analysis of the compound and evidently stimulated further work, for both Lau-

* Scientific Section, A. PH. A., Washington meeting, 1934.

rent (2) and Marchand (3) entered the field within the next three years, making silver picrate from silver carbonate and picric acid. Nothing further was done until Carey Lea (4), working in Philadelphia in 1858, prepared the chemical by interaction of silver nitrate and magnesium picrate and briefly described it and such of its properties as were then known, before the Society for the Advancement of Science.

There appears to be no further reference to silver picrate until 1905, when it is referred to in the literature of the time as being a new medicament of use in certain conditions of urethritis, vaginitis, etc., while Yale (5) claimed good results in the treatment of diphtheria. It was supplied for some time to the medical profession and exhibited in a gelatin or petrolatum base in the form of suppositories and ointments. It is due to numerous reports of its peculiar efficacy in these and allied conditions that our recent work has been stimulated.

The preparation of silver picrate according to the old and standard methods, such as the action of picric acid upon silver oxide or carbonate in aqueous suspension, has several disadvantages, mainly because of the low solubility of silver picrate in water, about one per cent at ordinary temperature. This necessitates the use of large volumes of liquid with consequent lengthy filtrations, evaporations, etc., in capacious tanks of special construction, if a satisfactory product is to be obtained. The solubility is somewhat higher (about 5%) in hot water, but application of heat is not desirable.

In a search for a solvent for silver picrate which would facilitate its preparation, most of the usual, and many unusual solvents were tried with but little encouragement, the maximum solubility being in most cases below one per cent. It is remarkable, therefore, to find that certain of the glycol ethers (particularly diethylene glycol monoethyl ether) possess remarkable solvent powers for this otherwise comparatively insoluble silver salt. We have by its means been able to prepare non-viscous solutions of silver picrate containing up to 40% of the solid which, while serving as a means of manipulation, may also be used directly as medicaments. In our new method of preparation use is made of this property of abnormal solubility, by carrying out the reaction in the glycol ether. Silver oxide is freshly precipitated in the usual way, washed, drained and pressed free from excessive moisture. It is then mixed thoroughly in a glass or enameled vessel with a sufficient quantity of the glycol ether to form a smooth paste. Picric acid is added in the stoichiometric proportion, when reaction takes place almost immediately and silver picrate is formed. On final warming to about 80° C. the liquid becomes practically clear, and is filtered when neutral to litmus. The bright golden liquid thus forms a concentrated solution of silver picrate, usually precalculated to give a concentration of about $33^1/_3\%$ of the solid. It may be used directly for the preparation of medicinal and pharmaceutical products or to prepare the solid in crystalline form. This operation consists in merely adding water to the concentrate and is the reverse of that usually employed in the preparation of crystalline substances, whereby water is gradually removed by evaporation. In this case by pouring the warmed glycol solution into about twice its volume of water, large and beautiful golden-yellow needles of silver picrate separate rapidly. These are drained, washed with ice water and air-dried with minimum exposure to light.

CHEMICAL AND PHYSICAL PROPERTIES.

Silver picrate thus obtained forms fine golden-yellow needles of intense coloring power, odorless, but possessing a penetrating bitter taste; the dust is somewhat irritating to nasal membrane. The bitterness and staining power are, however, much modified in solutions of the strength used in medications. The crystals usually separate with one molecule of water of crystallization but may, on occasion, be anhydrous. The substance contains about 30% of silver and is soluble, 1 part in 113 of water at room temperature; solubility at temperatures around 90° C. rises to about 5%. Boiling water or prolonged exposure of aqueous solutions to light result in gradual decomposition with separation of silver oxide, as is the case with many silver salts. The yellow color of the solutions, however, is some aid toward stability to light; colloidal silver chloride, for example, remains suspended in a solution of silver picrate without discoloration for many days, even in bright light. The solid detonates mildly on rapid heating, but it is not as violent; for example, as the sodium, potassium, ammonium or calcium salts. Silver picrate forms a well-defined compound with ammonia, first noted by Carey Lea (6) in 1861. By gradually adding ammonia solution to the glycol ether concentrate, no precipitation of silver oxide is formed, as might be expected. The solution turns deep orange and eventually precipitates long, thick, dark yellow needles of a compound which on analysis is shown to contain $2NH_3$ per molecule of silver salt. This substance possesses interesting properties which are still under investigation. It is not as stable as silver picrate, nor is it as soluble in water and other solvents. The solutions rapidly darken with separation of silver oxide or silver and the slightest application of heat causes the deposition of a shining silver mirror on containing vessels. If increase in bactericidal efficiency and therapeutic activity can be associated with this tendency to decomposition under ordinary circumstances, silver ammonio picrate should possess some interesting possibilities in therapeutic application.

The high solubility of silver picrate in the glycol ethers renders possible, in a simple and rapid manner, the formation of numerous ethers of picric acid. The required alkyl or aryl halide, such as ethyl iodide, phenyl chloride, etc., is merely dissolved in the same glycol solvent and added to the silver picrate solution. Silver halide is at once precipitated in the cold, practically quantitatively, leaving the required picric ether in solution. After filtering, water may be added to the liquid as previously described to produce fine crystals of the picric acid derivative. In this way methyl, ethyl, phenyl and benzyl picric ethers have been prepared with rapidity and ease. The method is not limited to organic derivatives, for metallic compounds may also be similarly produced. Mercuric chloride, for example, being soluble in the glycol ether, may be used to prepare mercuric compounds. It is hoped that this method may be extended to cover the preparation of other promising derivatives which are not readily obtained by the usual procedures.

PHARMACOLOGY AND BACTERIOLOGY.

From the pharmacologic and therapeutic standpoints silver picrate combines the effects of silver and of picric acid. It may be said to occupy an intermediate position having silver nitrate, with its caustic and irritating, but strongly germicidal properties on the one hand, and the non-irritating, mild, perhaps doubtfully germici-

dal, so-called colloidal silver preparations on the other. Silver picrate retains the medicinal qualities of the silver ion but possesses in addition, the well-known analgesic, healing and antiseptic properties of picric acid. Much of the bactericidal power is due to the silver which, although ionized in solution to a less extent than silver nitrate, makes silver picrate more efficient bactericidally than the colloidal silver or protein-masked products. The therapeutic properties of picric acid are well known, it having been used with success for many years in various skin lesions, including eczema, intertrigo, body ringworm, etc., Wilson (7) stating that in these particular complaints picric acid treatment gave results far superior to any other materials he had used. Kolmer (8) found that the use of picric acid as an application to the skin after vaccination proved four times more efficient than phenol in lessening the degree of local inflammatory action.

As an astringent, picric acid has been found superior to zinc sulphate or alum, while its penetrating powers are considerable, as shown by the fact that the hands are stained by the solution even through rubber gloves. Its use in burns and ulcers is well known, Muncy (9) stating that he had "failed to find an ulceration which did not respond to picric acid," while its "marked anodyne properties (when applied to wounds) made the use of aspirin or morphine rare."

In ophthalmic work, picric acid has met with approval, having been found "far superior in antiseptic action, in the strengths used, to other antiseptics usually administered in ophthalmology." Ehrenfried's (10) summation of the desirable therapeutic qualities of picric acid states the case particularly well:

> "Over any clean denuded surface it forms a protective aseptic scab by coagulation of secreted serum, which seals up ruptured lymph spaces, protects exposed nerve endings and splints the wound in such a manner that epithelial proliferation may proceed rapidly beneath, stimulating nature's method. This artificial scab protects against infection from external sources and promotes rapid and painless epidermatization."

If any corroboration of the above is required, Broon (11) reporting on results of picric acid in war surgery states:

> "One per cent picric acid is recommended for dressing superficial wounds, syringing sinuses, fractures and corroded tissues. It kills bacteria without corrosive effect and prevents suppuration, stimulates granulation of tissue, has marked anodyne properties and is less irritating and more efficacious than iodine. It may be used for sterilization of the skin in surgical cases and shortens the convalescent period."

In February of this year Stewart (12) reported his investigations into the maggot treatment of osteomyelitis, showing that a mixture of calcium carbonate and picric acid, or calcium picrate had practically the same effect as the maggots in stimulating phagocytosis and healing the wound. In the light of these and many other gratifying reports on the desirability and efficacy of picric acid, it would seem that silver picrate should be worthy of even greater consideration under similar circumstances. The additive effects of silver and picric acid would seem to be particularly desirable, as the action of the two constituents is apparently synergistic. The liberation of picric acid or picrates by interaction with tissue fluids should be preferable to the corrosive or caustic results of silver nitrate, particularly as the picrate radical would appear to exert such beneficial side effects. The irritating effects of silver picrate solutions in the concentrations normally used are insignifi-

cant, for in the course of this work silver picrate solutions of strength 1:1000 have been instilled into the eyes of dogs, cats and guinea pigs thrice daily for ten days and more without sign of irritation or deleterious effect. The solutions are less injurious than silver nitrate and definitely of greater efficacy and more rapid action than colloidal silver products. Baum (13) in testing a series of silver preparations including argyrol, protargol and silver picrate in several cases of gonorrhea, found that $^1/_4$ to $1^1/_2$% solutions of the picrate were as effective as 2 to 10% of some of the colloidal silver preparations in stopping the discharges present. By agar plate tests using typhosus, aureus, diphtheriæ and gonococcus organisms silver picrate was found to be the equal of similar strengths of silver nitrate in all cases but one (*C. diphtheriæ*). *Trichomonas Vaginalis*—the organism frequently found in cases of leucorrhea—is killed instantly by 1% silver picrate solutions, and pus cells are immediately coagulated. In short, silver picrate would appear to possess germicidal properties both physical and chemical in nature, picric acid apparently acting by precipitation of albuminous matter, and in some way denaturing the cell constituents. These effects, together with its powerfully penetrative properties, probably render the field more suitable for the subsequent action of the silver ion.

CLINICAL APPLICATIONS.

Silver picrate should be capable of application over a considerable therapeutic field, although with the exception of the recent work of Vanstane (14) who applied it successfully in *otitis media*, vaginitis, cervicitis, and diseases of the bladder, rectum and colon, its existence and usefulness appear to have been overlooked. The reason for this may possibly be accounted for by the number of reported fatalities among factory workers during the war period, resulting in the undeservedly restricted use of picric acid compounds.

The thought is therefore presented that, in the light of the above findings in which the combination of silver and picric acid has proved equal or superior to the usual silver medicaments without some of their disadvantages, this chemical should be worthy of recognition in medical and pharmaceutical armamentaria.

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DETERMINATION OF THE REASONABLE OR PERMISSIBLE MARGIN OF ERROR IN DISPENSING. III. SUPPOSITORIES.*

BY MARVIN J. ANDREWS.[1]

INTRODUCTION.

This, the third of a series of papers reporting the results of investigations made to determine what may be taken as the permissible margin of error in dispensing,[2] deals with suppositories.

Suppositories called for on prescriptions are usually prepared by mixing the active ingredients with the base in the solid state, then dividing and shaping

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[1] In collaboration with A. G. DuMez, Professor of Pharmacy, School of Pharmacy, University of Maryland. [2] JOUR. A. PH. A., 22 (1933), 755, 838; 23 (1934), 350, 421.

the resulting mass by hand; or by mixing the active ingredients with the melted base and pouring the mixture into molds to solidify. It is only in rare instances that suppositories are made by machine in the drug store. The vehicles commonly employed are cacao butter, glycerinated gelatin or sodium stearate.

For the purpose of this study, a typical suppository prescription was selected for compounding, and the suppositories were made by hand. Preparation of the suppositories by the other methods mentioned was not attempted as it appeared that these methods offered no additional possibilities for error, except the one due to a variation in the capacity of the individual molds. To discover if there was any appreciable variation in the capacities of the molds and to determine the effect of various methods of filling upon capacity, several series of experiments were carried out in which cacao butter alone was used.

EXPERIMENTAL PART.

The Pharmacopœia of the United States, Tenth Decennial Revision, page 366, gives the following information under suppositories:

"For suppositories made with Oil of Theobroma the following general processes may be employed:

Take of

The Medicinal Substance, the prescribed quantity.
Oil of Theobroma, grated, a sufficient quantity.

"Reduce the medicinal substance, if dry, to a very fine powder, or, if an extract, soften it with an appropriate liquid, then mix it thoroughly in a mortar with about an equal weight of grated oil of theobroma, and incorporate the remainder of the oil of theobroma until a homogeneous, plastic mass is obtained, adding if necessary, a small quantity of expressed oil of almond or wool fat. Roll the mass on a graduated tile until a cylinder of the proper length is formed, divide this into the required number of equal parts, and with a spatula, or other mechanical aid, form them into the desired shape.

"If the process of fusion is preferred, mix the medicinal substance with about an equal weight of grated oil of theobroma, as directed above, then thoroughly incorporate it with the remainder of the oil of theobroma, previously melted by a gentle heat on a water-bath, in a suitable vessel provided with a lip. Allow it to cool to about 38° C., and when the mixture begins to congeal, pour it immediately into suitable well-cooled molds. Keep the molds at a freezing temperature until the suppositories have hardened and are ready to be removed.

"Rectal suppositories should be cone shaped, and when made from oil of theobroma should weigh about 2 Gm."

Based on this information three series of tests were made. The first series of tests was carried out to determine the variation in weight and length of hand-made suppositories. The objective of the second series of tests was to determine the variation in capacities of the suppository molds used in the City of Baltimore in terms of cacao butter. The purpose of the third series of tests was to determine the effect, if any, of different methods of filling on the capacity of suppository molds.

With the first objective in view, the following prescription was filled, the suppositories being formed by hand.

℞ No. 1

Ext. Bellad.	Gm. 0.163
Pulv. Gall.	Gm. 1.300
Ol. Theobrom. *qs.*	Gm. 20.000

M. et ft. Supp. No. 10

In the actual performance of these tests, the suppository prescription was filled by 100 members of the senior class in dispensing pharmacy at the School of Pharmacy of the University of Maryland under working conditions described in the first paper. The completed suppositories were checked for accuracy with respect to weight by using a prescription balance, and for accuracy with respect to length by using a millimeter ruler. The standard deviation was computed from the results obtained.

In tests made to determine the variation in weight of suppositories prepared by hand, the students were instructed to follow the method outlined in the Pharmacopœia. In some instances a few drops of expressed oil of sweet almond, castor oil or a few grains of wool fat were added to the grated cacao butter. The suppository pipe was rolled and cut on a graduated tile. Some were prepared without the use of a dusting powder, while in others lycopodium or filter paper was used in the process of manufacture. The students were directed to make the suppositories cone shaped and to make them as near 25 mm. in length as possible.

The results of this series of tests are presented in Tables I and II.

TABLE I.—STANDARD DEVIATION IN WEIGHT OF SUPPOSITORIES MADE BY HAND.

Batch Number.	Av. Wt. in Gm.	S. D. in Gm.	Batch Number.	Av. Wt. in Gm.	S. D. in Gm.
1	1.791	0.106	51	1.774	0.151
2	1.946	0.079	52	1.954	0.133
3	2.025	0.401	53	2.130	0.291
4	2.009	0.066	54	2.183	0.064
5	1.713	0.160	55	1.677	0.114
6	1.840	0.189	56	2.047	0.068
7	2.236	0.167	57	1.631	0.318
8	2.049	0.413	58	2.157	0.353
9	1.952	0.045	59	2.015	0.029
10	2.068	0.095	60	1.915	0.143
11	2.117	0.210	61	1.867	0.067
12	1.911	0.063	62	2.054	0.178
13	1.555	0.354	63	2.349	0.314
14	1.710	0.205	64	1.863	0.046
15	1.999	0.182	65	2.094	0.167
16	2.034	0.166	66	1.982	0.092
17	1.934	0.143	67	1.690	0.235
18	2.025	0.095	68	2.046	0.154
19	1.960	0.169	69	2.000	0.418
20	2.044	0.089	70	2.032	0.421
21	1.943	0.124	71	2.351	0.310
22	2.008	0.162	72	2.214	0.273
23	2.010	0.113	73	2.244	0.117
24	2.081	0.279	74	1.984	0.170
25	2.017	0.049	75	1.883	0.097
26	1.765	0.227	76	2.153	0.083
27	1.876	0.071	77	1.939	0.088
28	1.894	0.052	78	1.935	0.071
29	1.721	0.221	79	2.041	0.284
30	1.844	0.128	80	1.850	0.139
31	1.853	0.256	81	1.760	0.157
32	2.193	0.225	82	1.815	0.279
33	2.161	0.258	83	1.845	0.020
34	1.683	0.238	84	1.974	0.179

35	2.071	0.462	85	2.048	0.195
36	1.683	0.252	86	2.036	0.229
37	1.843	0.222	87	2.039	0.133
38	1.959	0.090	88	1.979	0.183
39	1.819	0.134	89	1.638	0.039
40	2.256	0.235	90	1.863	0.067
41	1.905	0.084	91	1.880	0.126
42	2.051	0.085	92	1.860	0.155
43	1.886	0.194	93	1.994	0.126
44	1.962	0.210	94	1.877	0.269
45	1.942	0.189	95	2.008	0.192
46	1.919	0.122	96	1.940	0.214
47	2.064	0.049	97	2.185	0.451
48	1.913	0.065	98	1.926	0.061
49	1.830	0.188	99	1.873	0.093
50	2.176	0.121	100	2.121	0.119
			Average	1.959	0.172

In Table I it will be observed that in the case of the weight of the individual suppositories, the average standard deviation is 0.172 Gm., or 8.81 per cent based on the average weight. Fifty-eight of the batches compounded fall within the average standard deviation of 0.172 Gm., thirty-four fall within twice the average standard deviation, or 0.344 Gm., while eight fall within three times the average standard deviation or 0.516 Gm.

TABLE II.—AVERAGE LENGTH AND AVERAGE STANDARD DEVIATION IN LENGTH OF SUPPOSITORIES MADE BY HAND.

Number of Batches of Suppositories Prepared.	Average Length of Suppositories Prepared.	Average S. D. in Millimeters.
100	25.76 mm.	0.831

In Table II, it will be observed that in the case of the length of the individual suppositories the average standard deviation is 0.831 millimeters, or 3.30 per cent when based on the average length. On studying the original results it was noted that fifty-one of the batches compounded fell within the average standard deviation of 0.831 mm., forty-two fell within twice the average standard deviation, or 1.662 mm., while the remaining seven fell within three times the average standard deviation, or 2.493 mm.

For the purpose of making it possible to compare the results presented in Tables I and II with similar data that may have been published, but which have not been expressed in terms of the standard deviation, the per cent of deviation from the theoretical has been calculated and is given in Tables III and IV.

TABLE III.—PERCENTAGE DEVIATION OF HAND-MADE SUPPOSITORIES FROM THE THEORETICAL WEIGHT OF 2 GRAMS.

		Number of Suppositories in Each Batch That Deviate from the Theoretical by—				
Batch Number.	Average Weight in Gm.	5% or Less.	From 5% Plus to 10%.	From 10% Plus to 15%.	From 15% Plus to 20%.	Over 20%.
1	1.791	2	5	2	1	..
2	1.946	10	...	...	...	..
3	2.025	4	...	2	3	1
4	2.009	9	1	...	...	..

5	1.713	...	1	5	2	2
6	1.840	2	3	1	1	3
7	2.236	4	3	1	1	1
8	2.049	2	4	3	...	1
9	1.952	5	3	1	1	..
10	2.068	4	1	...	4	1
11	2.117	4	1	3	2	..
12	1.911	8	1	1	...	..
13	1.555	1	...	3	2	4
14	1.710	5	3	1	1	
15	1.999	4	2	4	...	..
16	2.034	4	4	1	1	..
17	1.934	7	1	1	1	..
18	2.025	8	1	1	...	..
19	1.960	2	6	1	1	..
20	2.044	8	2	...	...	
21	1.943	6	3	1	...	..
22	2.008	6	1	2	1	..
23	2.010	5	4	1	...	..
24	2.081	1	8	...	...	1
25	2.017	8	2	...	...	..
26	1.765	2	3	3	2	..
27	1.876	9	1	...	...	..
28	1.894	4	4	1	1	..
29	1.721	3	1	1	1	4
30	1.844	6	...	2	2	..
31	1.853	2	2	3	2	1
32	2.193	4	4	...	...	2
33	2.161	1	...	5	4	..
34	1.683	...	1	2	1	6
35	2.071	4	...	3	1	2
36	1.683	1	3	...	2	4
37	1.843	5	2	1	2	..
38	1.959	5	4	1	...	..
39	1.819	3	3	2	1	1
40	2.256	1	3	...	5	1
41	1.905	...	6	4	...	..
42	2.051	7	3	...	...	..
43	1.886	4	3	1	1	1
44	1.962	4	1	3	2	..
45	1.942	3	1	4	1	1
46	1.919	3	4	2	...	1
47	2.064	9	1	...	...	..
48	1.913	7	3	...	...	..
49	1.830	2	6	2	...	..
50	2.176	6	2	1	...	1
51	1.774	2	2	2	3	1

Batch Number.	Average Weight in Gm.	Number of Suppositories in Each Batch That Deviate from the Theoretical by— 5% or Less.	From 5% Plus to 10%.	From 10% Plus to 15%.	From 15% Plus to 20%.	Over 20%.
52	1.954	4	3	1	2	..
53	2.130	6	2	...	1	1
54	2.183	1	4	2	3	..
55	1.677	...	1	1	6	2
56	2.047	6	3	1	...	..

57	1.631	...	...	2	2	6
58	2.157	3	3	2	2	..
59	2.015	1	3	5	1	..
60	1.915	6	2	1	1	..
61	1.867	5	3	2	...	..
62	2.054	5	4	...	...	1
63	2.349	2	2	2	...	4
64	1.863	3	4	...	1	2
65	2.094	4	3	2	...	1
66	1.982	6	4	...	...	..
67	1.690	...	1	3	4	2
68	2.046	4	3	3	...	..
69	2.000	1	5	...	2	2
70	2.032	5	4	1	...	..
71	2.351	1	2	3	...	4
72	2.214	3	1	1	3	2
73	2.244	3	5	2	...	..
74	1.984	4	1	4	1	..
75	1.883	6	3	1	...	..
76	2.153	3	5	2	...	..
77	1.939	5	4	...	1	..
78	1.935	9	...	1	...	..
79	2.041	...	6	4	...	..
80	1.850	4	4	...	1	1
81	1.760	2	2	2	2	2
82	1.815	5	1	1	2	1
83	1.845	...	10	...	...	..
84	1.974	3	3	4	...	..
85	2.048	3	3	1	3	..
86	2.036	7	2	1	...	..
87	2.039	6	2	2	...	..
88	1.979	3	5	1	1	..
89	1.638	...	...	2	7	1
90	1.863	2	5	3	...	..
91	1.880	6	3	...	...	1
92	1.860	7	2	1	...	..
93	1.994	5	4	1	...	..
94	1.877	4	3	2	1	..
95	2.008	3	4	3	...	..
96	1.940	6	3	1	...	..
97	2.185	4	1	1	...	4
98	1.926	6	3	1	...	..
99	1.873	4	4	2	...	..
100	2.121	3	3	2	2	..
	Totals	395	271	155	102	77

The data presented in Table III show that for a total of 1000 hand-made suppositories prepared by 100 different operators, 66.6 per cent fall within a deviation of 10 per cent of the theoretical weight, 82.1 per cent fall within 15 per cent, while 92.3 per cent fall within 20 per cent.

VARIATION IN CAPACITY OF SUPPOSITORY MOLDS IN TERMS OF CACAO BUTTER.

A second series of tests was carried out to determine to what extent suppository molds used in retail pharmacies in the City of Baltimore varied in capacity.

TABLE IV.—PERCENTAGE DEVIATION OF HAND-MADE SUPPOSITORIES FROM THE THEORETICAL LENGTH OF 25 MILLIMETERS.

Number of Suppositories Prepared.	Number of Suppositories That Deviated from the Theoretical Length by—				
	5% or Less.	From 5% Plus to 10%.	From 10% Plus to 15%.	From 15% Plus to 20%.	20% or Over.
1000	624	214	124	37	1

The percentage deviation from the theoretical length of 25 millimeters show that 62.4 per cent fall within 5 per cent, 83.8 per cent fall within 10 per cent, 96.2 per cent fall within 15 per cent, while 99.9 per cent fall within 20 per cent.

For these tests, ten different sets of suppository molds were borrowed at random from retail drug stores and the capacities of the individual molds determined in terms of cacao butter.

To obtain the desired data, suppositories of cacao butter were prepared by fusion in each of the ten sets of molds borrowed. The melted cacao butter was cooled to the congealing point and then poured into the well-cooled molds. The excess was removed by running the edge of a spatula over the top of the molds immediately after the cacao butter had solidified. The individual suppositories were then weighed and the weights recorded.

A summary of the results of the second series of tests is given in Table V.

TABLE V.—CAPACITY OF SUPPOSITORY MOLDS IN TERMS OF CACAO BUTTER.

No. of Sets of Molds.	Av. Capacity in Gm.	S. D. in Gm.	No. of Sets of Molds.	Av. Capacity in Gm.	S. D. in Gm.
1	1.493	0.008	6	2.032	0.022
2	2.095	0.009	7	1.390	0.027
3	1.915	0.026	8	1.975	0.023
4	1.887	0.014	9	1.481	0.051
5	2.400	0.023	10	1.318	0.037
			Average	1.798	0.024

The data obtained in this series of tests show that the weight of individual suppositories made with the ten sets of borrowed molds range from a low of 1.255 Gm. (in mold No. 10) to a high of 2.440 Gm. (in mold No. 5), or a difference of 1.185 Gm.

The average capacity in grams in terms of cacao butter of all of the ten sets of suppository molds as shown in the table is 1.798 Gm., while the average standard deviation is 0.024 Gm. On further study of the table it will be observed that the deviations for six of the sets of molds fall within the average standard deviation of 0.024 Gm., three fall within twice the average standard deviation or 0.048 Gm., while only one falls within three times the average standard deviation or 0.072 Gm.

To make it possible to compare the results presented in Table V with similar data that may have been published but which have not been expressed in terms of the standard deviation, the per cent of deviation has been calculated.

The weights of the individual suppositories showed the variation from the average to be less than 5 per cent in every instance, except for the suppositories prepared with mold No. 9. In the latter case the weight of 90 per cent of the suppositories fell within 5 per cent of the average weight, while in the remaining 10 per cent there was a variation of 9.8 per cent from the average weight. On ex-

amination, it was discovered that some of the individual molds of this set were bored deeper than others.

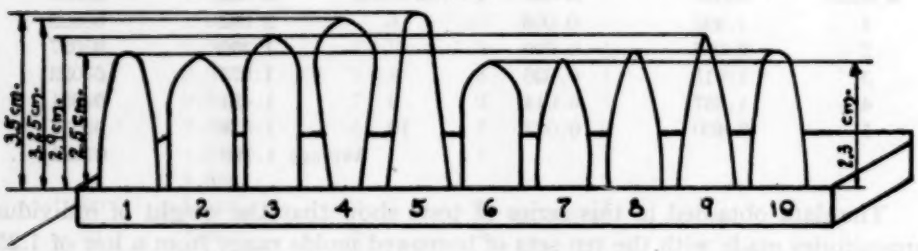
The per cent deviation from the theoretical weight of 2 Gm. of cacao butter has also been calculated, the results are given in Table VI.

TABLE VI.—PERCENTAGE DEVIATION BASED ON THE THEORETICAL WEIGHT OF 2 GM. OF CACAO BUTTER.

No. of Sets of Molds.	Percentage of Individual Suppositories Deviating from 2 Gm. by— 5% or Less.	From 5% Plus to 10%.	From 10% Plus to 15%.	From 15% Plus to 20%.	From 20% Plus to 25%.	25% or More.
1	.....	....	....	....	60%	40%
2	87.5%	12.5%	....	....	....	...
3	75.0%	25.0%	....	....	....	...
4	50.0%	50.0%	....	....	....	...
5	.....	....	....	62.5%	37.5%	...
6	100%	...	....	....	....	...
7	.....	....	....	....	40.0%	60%
8	100%	....	....	....	....	...
9	.....	....	....	....	40.0%	60%
10	.....	....	....	....	....	100%

The variation in length and the difference in shape of the suppositories pre pared with the ten sets of suppository molds used are shown in Table VII.

TABLE VII.—VARIATION IN LENGTH AND SHAPE OF SUPPOSITORIES PREPARED IN THE 10 SETS OF MOLDS.



EFFECT OF DIFFERENT METHODS OF FILLING ON THE CAPACITIES OF SUPPOSITORY MOLDS.

A third series of tests was carried out to determine to what extent, if any, the capacity of suppository molds is affected by the method of filling. With this objective in view suppositories of cacao butter were prepared in the same mold by each of the following methods:

1. Melting and pouring cacao butter into well-chilled molds.
2. Preparing rough suppositories by hand, then forcing them into the mold to obtain a uniform shape.
3. Preparing suppositories by compression in a suppository machine.

The results of this series of tests are presented in Table VIII.

TABLE VIII.—EFFECT OF THE METHOD OF FILLING ON THE CAPACITIES OF SUPPOSITORY MOLDS.

Method of Preparation.	Capacity in Gm. of Cacao Butter. 1.	2.	3.	4.	Average Capacity in Gm.	S. D. in Gm.	Per Cent Deviation.
Melting and pouring into mold	2.300	2.305	2.305	2.285	2.298	0.008	0.34%
Massed and forced into mold	2.200	2.220	2.300	2.225	2.236	0.037	1.70%
Made by compression in machine	2.395	2.390	2.380	2.345	2.377	0.019	0.79%

An examination of the results in Table VIII shows that the method of filling has a definite influence upon the capacities of suppository molds. Based on the results obtained it may be stated that the capacity in grams of cacao butter, beginning with the smallest and ending with the largest, varies in accordance with the following order of arrangement: (1) Suppositories prepared by hand and then forced into the molds to shape; (2) suppositories prepared by melting the ingredients, then pouring into well-chilled molds and allowing to solidify and (3) those made by compression in a suppository machine. Likewise, it will be found that the greatest variation in weight occurs in the suppositories prepared by hand and forced into the molds to shape, while the most uniform are those prepared by fusion.

The variation in capacity due to a difference in the method of filling the molds as observed in the above tests was surprisingly small being less than 2 per cent for all suppositories except in the case of those prepared by hand and then forced into the molds when it was less than 3.5 per cent. All of the suppositories in this series fall within twice the standard deviation.

CONCLUSIONS.

1. The weight of suppositories prepared by hand varies with the working temperature, the technique of the individual operator and the size and shape of the suppository to be prepared.

2. The results of the first series of experiments show that 92 per cent of a total of 1000 different suppositories prepared by 100 different operators fall within twice the average standard deviation for weight of 0.344 Gm. This corresponds to a variation of 17.2 per cent when based upon the theoretical weight of 2 Gm.

3. The results of our experiments showed that there is no greater variation in length than in weight of suppositories made by hand if a definite length is decided upon. In ordinary practice, however, this is not true as there are no official standards for length, and each pharmacist makes his own standards.

4. Individual suppositories in a set of molds do not vary in capacity beyond reasonable limits. There was observed, however, a great variation in the capacity of the sets of suppository molds as used in different retail drug stores. The latter variation is believed to be due to the fact that the manufacturers of suppository molds do not have any definite specifications to follow.

5. A difference in the method of filling was observed to have an appreciable effect upon the capacities of suppository molds.

(*To be continued.*)

THE OPENING SESSION.

Time has once more brought us round to the renewal of those medical studies of which pharmacy is a branch. Year by year it assumes a more definite character; and the period is not far distant when both in teaching and in practice it will occupy an independent place. At Bloomsbury Square, where official pharmacy is enshrined, history was seen to repeat itself; there was the same crowd of visitors and friends to welcome successful candidates; the same band of young aspirants who had gained distinction; the same professional congratulations; and a lecturer to give the accustomed introduction address. Retrospect of Fifty Years Ago.—*The Chemist and Druggist*, October 15, 1884.

A PHYTOCHEMICAL STUDY OF CANCHALAGUA PANAMENA.*

BY ROBERTO A. BENEDETTI.[1]

Canchalagua Panamena, very much like the *Erythræa chilensis*, Pers. is a Gentianaceæ of the species *Schultesia lisianthoides* (Paul Standley). It grows in the Savannas just outside of Panama City.

The plant, *Canchalagua Panamena*, varies from 7 cm. to 30 cm. in height, the stem is quadrangular throughout with branches opposite. The leaves are linear and opposite consisting of five nerves. The dirty pink solitary flower is about 15 mm. long and it comes out of an elongated capsule which later contains the numerous tiny seeds. All parts of the plant have a very bitter taste.

For many years the farmers in the Interior of the Republic of Panama have used Canchalagua as a febrifuge. The therapeutic use of the drug is that of a febrifuge in malarial fevers, as a tonic, and for regulating the liver against jaundice. The therapeutic dosage is, as a tonic, 120 cc. of a 1% infusion; as an anti-icteric and febrifuge 240 cc. of a 3% infusion. The soft extract may be used in doses from 0.20 cg. to 1 Gm. and the powdered drug from 1 Gm. to 5 Gm.

A representative sample of the entire plant was analyzed according to the U. S. P. methods with the following results:

Total ash	5.67%
Moisture (for non-volatile constituents)	9.27%
Alcohol-soluble extractive	9.58%
Diluted alcohol-soluble extractive	12.50%
Water-soluble extractive	9.97%

A 25-Gm. sample of the air-dried drug was reduced almost to a powdered form and extracted in a Soxhlet extraction apparatus with several solvents. Ether, ethyl alcohol and water were the solvents used and in the order mentioned.

The ethereal extraction was acid to litmus paper, taste, bitterless; color, emerald green. The ether was evaporated from the extract and a solid-like mass was obtained weighing 1.31 Gm. (5.24% of the drug). The extract had a waxy appearance and tasted like wax.

The bitter alcoholic extraction gave an acid reaction with litmus paper. A few cc. of the extract showed a beautiful emerald green coloration, but a larger quantity was reddish brown. The alcoholic extract was tested for alkaloids with Mayer's reagent and picric acid giving negative results. The extract, after evaporation to a glucose consistency, weighed 5.52 Gm. (22.08% of the drug). In order to obtain a purer product, the extract was treated 3 times with a mixture of 20 cc. of ether, 5 cc. of alcohol and 15 cc. of water in a separatory funnel. The water solution from the separatory funnel was evaporated—the reddish brown jelly like substance obtained was intensely bitter, acid in reaction and insoluble in ether. This mixture was then treated with ethyl alcohol in which most of the extract dissolved. The filtrate was evaporated to determine if crystals would be formed, but unsuccessfully; a reddish brown jelly-like substance separated. This substance was intensely bitter, acid to litmus paper and when hydrolyzed with dilute hydrochloric acid reduced Fehling's solution.

The aqueous extract from the Soxhlet extractor was acid to litmus paper. Its solution tastes bitter when fresh, but on standing becomes practically bitterless. The reddish brown extract was evaporated to a solid-like consistency and weighed 3.45 Gm. (13.80% of the drug).

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* Joint Session, Scientific Section and Section on Practical Pharmacy and Dispensing, A. PH. A., Washington meeting, 1934.

[1] Panama City, Panama.

The extract showed the absence of alkaloids. After dissolving the extract in a little distilled water and then diluting with ethyl alcohol a bitterless brown gum precipitated.

A 10 per cent infusion of the drug was acid to litmus paper and reduced Fehling's solution, showing that it contained a free acid and glucose. A few drops of Ferric Chloride solution added to the infusion gave an ink.

About 16 Gm. of cut Canchalagua was percolated with ethyl alcohol. A part of the percolate, after concentration, failed to reduce Fehling's solution. Then another portion of the percolate, 30 cc., after being boiled for one-half hour with 2 cc. of a 5% hydrochloric acid reduced Fehling's solution. This reaction showed the presence of a glucoside.

Several methods were employed to obtain a glucoside but without success, probably due to the small quantities of drug used. In one of the methods, the drug was boiled with milk of lime to remove the tannin. The filtrate, after evaporation to a soft extract, was digested with ethyl alcohol and filtered; to this, ether was added, but no precipitation was obtained.

CONCLUSIONS.

1. *Canchalagua Panamena* resembles *Erythræa chilensis* physically and therapeutically.
2. Uses of the drug: febrifuge, anti-icteric and tonic.
3. The most important constituents of the drug are: a bitter glucoside, free acid, a sugar, wax, gum, tannin and green coloring matter.

REFERENCES.

1. "Oficina de Farmacia de Pontes."
2. "Flora of the Panama Canal Zone," by P. Standley.
3. "Materia Medica," by D. Culbreth.
4. "Elementos de Materia Farmaceutica," de J. G. Pamo.

NOTE: I wish to thank Professor M. J. Andrews of the University of Maryland for asking me to write this paper, and also Brother Higino and A. F. Alba, Herbalists of Colegio La Salle in Panama City, for their coöperation in the classification of the drug.

SOME TIMELY FORMULAS FOR THE CHIROPODIST.*

BY ADOLPH F. MARQUIER.

It has always been a fitting effort on the part of the pharmacist to prepare for the members of the healing art, suitable medicinal preparations to meet the various conditions that present themselves daily. In the past and the present we have and are giving considerable time and thought to the human machine and its ailments but our feet only in recent years are receiving scientific consideration and in the writer's opinion there is a great future in this line of endeavor. There are at present a number of formulas in use by the practitioners of this art and the writer is taking the liberty of submitting a few of the formulas which in experience have proven some value.

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* Section on Education and Legislation, A. PH. A., Washington meeting, 1934.

SOLUTION OF ALUMINUM CHLORIDE COMPOUND.

Aluminum Chloride	**50.0 Gm.**
Alcohol	**120.0 cc.**
Oil Lavender Flowers	**0.6 cc.**
Tincture of Cudbear	**0.6 cc.**
Water	
To make	**500.0 cc.**

Use for Bromidrosis.

Directions: Apply at night and morning.

SPIRIT OF MENTHOL COMPOUND.

Menthol		**4.0 Gm.**
Camphor		**4.0 Gm.**
Oil Lavender		
Oil Bergamot	of each	**1.5 cc.**
Oil of Orange Flowers		**0.3 cc.**
Alcohol 70%		**500.0 cc.**

Mild counter irritant and refrigerant.

SPIRIT OF THYMOL COMPOUND.

Benzoic Acid	**8.0 Gm.**
Salicylic Acid	**8.0 Gm.**
Thymol	**5.0 Gm.**
Methylene Blue	**0.120 Gm.**
Oil Neroli	**0.300 cc.**
Alcohol 70%	**500.0 cc.**

Epidermophytosis—Athlete's Foot.

We have had official for a number of years the salicylic acid, Indian Hemp, collodion, Whitfield Ointment, compound talc powder, inunction menthol comp., Stainless Iodine Ointment. All of these preparations are extensively used by both the doctors and the laity.

AN ENTERIC COATING FOR TABLETS.*

HAROLD A. JOHNSON[1] AND RALPH W. CLARK.[2]

The writers have reviewed the more commonly used American textbooks as well as journal literature searching for references on enteric coatings for pills, capsules and tablets. Salol or mixtures of salol with other substances seem to be the materials favored by most writers. Salol is made use of in certain commercial enteric coated tablets. Enteric coated Glycotauro tablets are coated with salol (1), enteric coated tablets, Neutral Acriflavine-Abbott, are coated with shellac and salol while enteric coated tablets, Neutral Acriflavine-National, are coated with salol containing some keratin (2). Several methods of applying salol coatings to pills and capsules have been suggested. Apparently, however, little work has been done on developing a method of applying a salol coating to tablets in a manner which

* Section on Practical Pharmacy and Dispensing, A. PH. A., Washington meeting, 1934.

[1] Senior Student in Pharmacy, University of Wisconsin.

[2] Instructor in Pharmacy, University of Wisconsin.

could be used satisfactorily by the retail pharmacist. The present paper deals with a simple method of salol coating tablets.

Pills, capsules and tablets are the accepted modes of administration of medicines which need only to be taken in small quantities. They are used to advantage for bad tasting drugs. Pills and tablets may be coated to further disguise bad tastes and all three modes of administration may be coated in such a manner as to make them reach the intestines before they dissolve or disintegrate. Capsules may also be treated with formaldehyde to render the gelatin insoluble in the acid juices of the stomach.

Pills, one of the oldest forms in which medicines are given, were probably first experimented with in an attempt to secure an enteric coating. In 1884 Dr. Unna (3) experimented with keratin as an enteric coating. Keratin is now generally held as of little value for this purpose. Previous to 1884 fatty and resinous substances had been employed (4). Beginning with the third edition, the National Formulary has given a method of salol coating pills by rotating them in successive, small amounts of salol, thus applying several thin coats. Salol or a mixture of salol with other substances may be applied in liquid form by spraying a solution on the pills while agitating them in a suitable dish.

An enteric coating may be applied to capsules by similar methods. However, Cook and LaWall, in the seventh edition of Remington's Practice of Pharmacy (5), point out that greater care is necessary to secure complete coating. They also state that the capsules being flexible and the coating very brittle, it is necessary to handle them with care to avoid cracking off the coating. Husa and Magid (6) came to the conclusion that a coating applied by spraying a mixture of salol, stearic acid and an alcoholic solution of shellac is satisfactory. Bukey and Rhodes (7) studied the treatment of gelatin with formaldehyde and recommend as a method to be used by the pharmacist an immersion for 5 to 15 seconds in a 10% formaldehyde solution. They also used gelatin-coated pills in their study.

Tablets may be coated by spraying a solution of the material or materials upon them while they are being agitated. Wruble (8) developed a coating consisting of shellac, suitable for large scale production. He made use of a 25% solution in equal quantities of alcohol and ammonia. Because of their shape, tablets, like capsules, do not lend themselves to the National Formulary and similar methods of coating. Therefore the following method for salol coating of tablets has been developed. Although this method is not all that is to be desired, it may be used to coat a dozen tablets in about one-half hour's time after the operator becomes familiar with the technique involved.

A METHOD FOR SALOL COATING TABLETS.

Melt a sufficient quantity of salol in a 4-inch casserole on a water-bath to completely cover a tablet upon dipping it into the melted salol. When the melted salol reaches the temperature of from 45–50° C. (salol melts between 41–43° C.), grasp the tablet to be coated on its narrow sides with a pair of tweezers, the points of which have been bent inward, and dip the tablet into the melted salol. Remove and keep the tablet moving in a circular motion in the air until the salol congeals. Shift the tweezers to a new position on the tablet and repeat the operation until a coating of the desired thickness is obtained. Usually three dippings are enough.

To make the coating smooth and glossy, grasp the coated tablet with tweezers and pass it quickly through a Bunsen flame.

Test tablets containing methylene blue and calcium sulphide for determining the effectiveness of the coatings were prepared by the formula used by Wruble (9). The tablets were compressed on a Stokes hand-operated tablet machine. As considerable inconvenience was experienced with Wruble's formula, the following was developed with no changes in the quantities of the two active ingredients:

Methylene blue	1/4 grain
Calcium sulphide	1/2 grain
Lactose	3/4 grain
Starch	1 1/2 grain
Purified talc.	1 1/4 grain
Sugar	3/4 grain

Granulate with a gelatin solution prepared as follows:

Pour upon 180 grains of gelatin sufficient water to cover it and allow it to stand one hour, then pour off the water. Transfer the washed gelatin to a dish, add 240 minims of glycerin and sufficient water to make four fluidounces. Heat on a water-bath until the gelatin is dissolved. Use while warm.

There is some question about the effectiveness of these tablets for testing enteric coatings as several students reported no eructations of hydrogen sulphide after taking the uncoated tablet.

The test tablets were coated with the salol as described above. Sixty students were each asked to take one of these tablets. Five reported eructations of hydrogen sulphide gas. Three reported no reaction. The balance of the group reported blue coloration of the urine. This is evidence that the salol coating does not dissolve in the stomach, but dissolves in the intestinal fluids allowing the tablet to disintegrate there.

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(3) P. G. Unna, *Pharm. Zentralh.*, 25 (1884), 577; from *Fortschr. Med.*, 15 (1884), 507 and Jour. A. Ph. A., 10 (1921), 372.

(4) A. G. DuMez, Jour. A. Ph. A., 10 (1921), 372.

(5) E. F. Cook and C. H. LaWall, "Remington's Practice of Pharmacy," 7th Edition (1926), 1683.

(6) W. J. Husa and L. Magid, Jour. A. Ph. A., 21 (1932), 1030.

(7) F. S. Bukey and P. Rhodes, *Ibid.*, 22 (1933), 1253.

(8) M. S. Wruble, *Amer. J. Pharm.*, 102 (1930), 326. (9) *Ibid.*, 327.

Wholesale Drug Analysis.—An analysis of wholesale drug operations, based on an eight months' study of a typical wholesaling establishment, has been published by the Bureau of Foreign and Domestic Commerce of the Department of Commerce as a bulletin—"Domestic Commerce Series—No. 86." The work reported was supervised by Wroe Alderson on a plan laid out by John R. Bromell. The study was made and the report prepared by Edward J. Carroll. Detailed statistical records and comment are given on selling, buying, commodity coverage, storage, transportation, finance and risk bearing, a comparative tabulation being included which covers eight types of drug wholesaling. The data are broken down for departments, and although the author disclaims any purpose of critically analyzing the trade as a whole, his records, being factual have a wide relative value. The bulletin comprises 110 pages. It is for sale by the Superintendent of Documents, Government Printing Office, Washington, at 15 cents a copy.

MEDICAL AND PHARMACEUTICAL CONTRIBUTIONS TO ELECTRICAL SCIENCE.*

BY CHARLES WHITEBREAD.[1]

Pharmacy and medicine have played an important rôle in the development of electrical science because pharmacists and physicians were among the first to make practical use of this agency, and because it was the discoveries, studies and writings of these men which furnished the impetus for the early investigations and researches that have made electricity the agency for good which it is to-day.

Our science, and science generally, does not need champions to proclaim the part taken in human progress, as the accomplishments of the past and of the present speak for themselves. It is a human failing, however, to accept the benefits which come to us as the direct result of the scientific investigations which have made the forces of Nature our servants, and to forget the part taken by mankind to make possible the comforts and conveniences which we now enjoy. Let us, therefore, see how we obtained the fundamentals of our knowledge of electricity, noting particularly the contributions of our own and affiliated professions, and how medicine generally has benefited from a branch of science based in no small degree on the discoveries of medical men.

The earliest mention of electricity is supposed to have been made by the Ionian philosopher, Thales of Miletus, who died about 548 B.C., and who discovered that if a piece of smooth amber is rubbed with a dry cloth it attracts light bodies placed near it. Although Thales was regarded as one of the seven wise men of ancient Greece, it is recorded of him that he thought amber possessed a soul, and that it was nourished by substances which it attracted to itself. Natural magnets were known in Europe more than two thousand years ago, and the Chinese have used them since 600 B.C. They were portions of lodestone, native oxide of iron, and the word magnet came into use because this ore was found in Magnesia, Asia Minor.

The observations of Thales concerning amber, and of others relative to the magnet, remained without development until the 16th century, when Dr. William Gilbert, physician to Queen Elizabeth of England, published a treatise on the magnet in the year 1600, giving the results of the experiments which he had conducted up to that time. This physician was the discoverer of frictional electricity in a large number of substances; of static electricity; the repulsion of similar and the attraction of dissimilar poles of the magnet; the diversion of the magnetic needle by electricity; the strengthening of a magnet by an armature; the fact that iron bars become magnetic along the magnetic meridian; that the earth itself is an enormous magnet, etc. We are also indebted to Dr. Gilbert for the name electricity which was derived from a Greek word meaning amber, and his investigations of a subject which had lain dormant for more than two thousand years, marked the inauguration of the experiments and researches which have since added so greatly to our fund of knowledge.

A German scientist, Otto vonGuericke (1602–1688), made the first electric machine, which consisted of a globe of sulphur on an axis mounted in a frame,

* Section on Historical Pharmacy, A. PH. A., Washington meeting, 1934.

[1] Assistant Curator, Division of Medicine, U. S. National Museum.

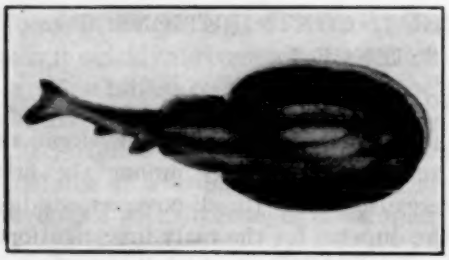

Fig. 1.—The Electric Ray (*Torpedo galvani*). This fish, common in the tropical seas, was the source of the static electricity first employed in the treatment of disease. It was an animal drug at the beginning of the Christian Era.

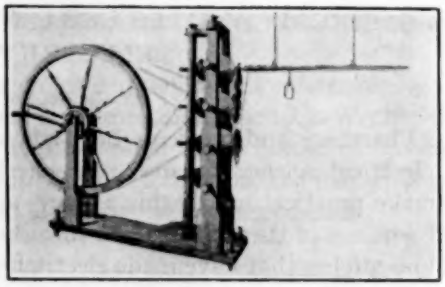

Fig. 3.—Dr. Watson's Electric Machine. The mechanical rubbers are to the left of the globes, and the conductor is suspended by silk cords on the right. (From Priestley's "History of Electricity," 1775.)

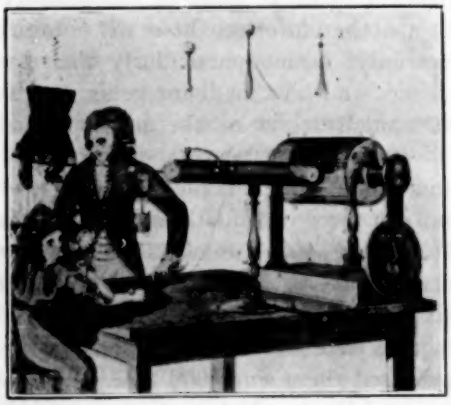

Fig. 4.—Administration of static electricity. (From a print published in 1799.)

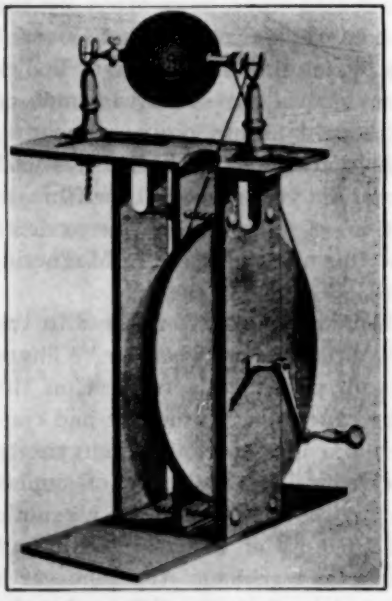

Fig. 2.—Hawksbee's Electric Machine. An early improvement on the first electric machine made by von-Guericke. (From Priestley's "History of Electricity," 1775.)

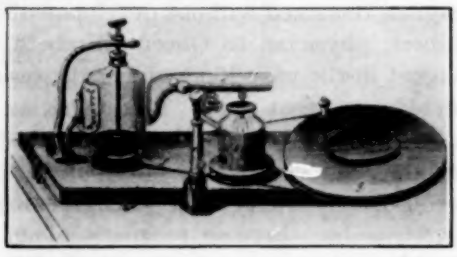

Fig. 5.—Read's Cylinder Machine. One of the early types of electric machines especially constructed for medical purposes. (From Priestley's "History of Electricity," 1775.)

and discovered the electric spark, observing the crackling sound which accompanies it. Francis Hawksbee, in 1709, improved the electric machine, substituting a globe of glass for vonGuericke's sulphur globe. In both of these machines the

hand was used to supply the necessary friction, but it was not long before a mechanical rubber and a prime conductor were added to the apparatus. The frictional electric machine was improved by others, and soon a special machine for medical purposes was in use.

In 1729, Stephen Gray, while experimenting with a medicated tube, found that he could convey an electrical charge to a distance by a hemp string. Later he found that when a wire 700 feet long, and hung on loops of silk, was connected at one end with the glass tube, and the tube was rubbed, the other end was electrified and would attract light bodies. This discovery was the first to introduce the distinction between conductors and non-conductors, and was the origin of our knowledge of insulators.

In 1745, the properties of the leyden jar—so-called because many of the early experiments were conducted at the University of Leyden, Holland—were discovered by vonKleist, Cuneus, Allamand and Muschenbroek, and affirmatively answered the question: "Can electricity be stored?" Sir William Watson, M.D., in 1747 and 1748 took part in the experiments by which an electrical discharge from a leyden jar was "extended to four miles in order to prove the velocity of its transmission."

In America, Benjamin Franklin distinguished between positive and negative electricity, in 1747, and demonstrated the identity of the electric spark and lightning in 1752. He also devised the lightning rod, and took such an active part in the study of frictional electricity that it is sometimes called franklinic electricity.

Up to this time researches had been confined to studies of static or frictional electricity, that is, electricity in a condition or state of rest, but in 1791, an Italian physician and professor of anatomy, Luigi Galvani, by his famous frog experiments, laid the basis for the discovery of dynamic electricity, that is, electricity in motion. An Italian physicist, Alessandro Volta, when following up the work of Galvani, in 1799, devised the voltaic pile, the first electric battery. Volta's pile, a vertical column of several pairs of zinc and copper disks separated by moist cloths, supplied the knowledge that electricity is generated by chemical action. This pile was found to be charged with positive electricity at its lower extremity and with negative electricity at the upper extremity. When wires attached to these extremities were brought into communication with each other and then separated, a minute spark was observed which corresponded to the spark obtained from the frictional electric machine. Electricity produced by Volta's pile was called voltaic, galvanic, battery or primary electricity.

Until the year 1820 electricity and magnetism were regarded as distinctly separate sciences, but in this year Hans Christian Oersted,[1] a professor of physics at Copenhagen, proved the intimate relationship between the two, when he observed that a wire in which a voltaic current was passing deflected a magnetic needle suspended near it. Oersted's experiments and those which followed by Ampere, Weber, Arago and Sturgeon marked the discovery of electro-magnetism, and introduced an important era of electrical research which was participated in by many eminent authorities. Michael Faraday, in England, and Joseph Henry, in the United States, almost simultaneously made the discoveries that gave us

[1] Son of a pharmacist—see JOUR. A. PH. A., April 1931, page 370.

our knowledge of induced currents, and furnished the fundamental information which made possible the modern era in the history of electricity.

Among the earliest applications of electricity to human welfare was its use in the treatment of disease. The compass was of great service in navigation, and Franklin's rods had provided a safe method of protecting buildings from lightning. The real advances in the way of putting electricity to practical use, however, only date from the time of Faraday and Henry, the great men who, by their experiments and researches, made possible many of the conveniences which we enjoy to-day. One of the first of these modern applications was telegraphy; the telephone was another; and magneto-electric and dynamo-electric generators and motors are now so common that we are inclined to forget that their introduction has taken just about a century.

The practical applications of electricity have come with such rapidity since the days of Faraday and Henry that they cannot be considered in this brief article. With the fundamental discoveries in mind, and a recollection that materia medica specimens were the chief source of electricity in the early days; that search for a means of curing disease stimulated investigation; and that medical men were leaders in electric experimentation, we can now turn our attention to a consideration of electrotherapy.

The treatment of disease by electricity is called electrotherapy, and if the earliest employment of remedial substances whose real or supposed efficacy depended on electrical phenomena are included under this term, electrotherapy can claim an antiquity as great as some of the oldest branches of medical science. The fish known as the "electric ray," common in the tropical seas, was the source of the static electricity first employed in the treatment of disease. A Roman compiler of materia medica, Scribonius Largus (14–54 A.D.), was the first to recommend the use of electric shock as communicated by this fish in the treatment of severe headaches. Galen, "The Father of Pharmacy," and the most famous of the Græco-Roman physicians at the beginning of the Christian era, also prescribed shocks from the "electric ray" for the cure of headache, and classical writers of this time spoke of this form of medication in cases of cramp, paralysis, gout, diseases of the joints and disorders of nervous origin. In his "Natural History" Pliny refers to the electric ray as if its use as a therapeutic agent was quite general. He says: "From a considerable distance, even, and if only touched with the end of a spear or staff, this fish has the property of benumbing the most vigorous arm, and of riveting the feet of the runner, however swift he may be in the race. If, upon considering this fresh illustration, we find ourselves compelled to admit that there is in existence a certain power, which by the very exhalations, and, as it were, emanations therefrom, is enabled to affect the members of the human body, what are we not to hope for from the remedial influences which Nature has centered in all animated beings?" Later on, the *Gymnotus electricus*, or electric eel of South America, was of interest as the subject of much experimentation because it was able to administer a much more powerful shock than the electric ray.

The natural magnet, or lodestone, was a form of primitive electrotherapy, which comes under the heading of magic medicine, as whatever effect was produced by holding it in the hand or wearing it suspended from the neck must have been a psychological one which arose from the superstitious belief that the characteristic

properties of the magnet gave it the power to attract or repel the causes of disease. The oldest account of the use of the magnet in medicine is ascribed to Aetius, physician to Justinian I (A.D. 527–565), who said: "We are assured that those who are troubled with the gout in their hands or feet, or with convulsions, find relief when they hold a magnet in their hand." Johannes Arculanus, a professor at Bologna and Padua during the 15th century, is said to have endeavored to remove splinters of iron from the eye by means of the attraction of amber electrified by friction. Paracelsus, one of the most famous of the 16th century European physicians, made use of the magnet in the treatment of toothache and other disorders. Later it was used in the treatment of headache, and magnetic toothpicks and earpicks were extolled as remedies for disorders of the teeth and ears, and Kircher (1598–1680) speaks of the magnet being worn about the neck to prevent convulsions and nervous diseases. While most of these early attempts to utilize a force concerning which little was known were based on "the influence of imagination in the cure of disease," still they served the very good purpose of keeping alive the interest in electrical science and electrotherapeutics.

The electrotherapy of the 18th century was confined to the electrification of patients and the administration of shocks by means of electric machines and leyden jars. Professor Jallabert, of Geneva, in 1748, noticed the phenomenon of muscular contraction resulting from electric stimulation, and Professor Kratzenstein (1723–1795), was among the first to employ electricity produced by these methods successfully, it being recorded that after fifteen minutes of electrification he cured a woman suffering with a contraction of the little finger. Rossler introduced the electric bath as a remedial agent in 1768; Manduyt, in 1777, employed electricity in the treatment of amblyopia; Charles Darwin used it as a remedy for jaundice; and Hufeland recommended electricity for the relief of asphyxia.

Exaggerated accounts of great cures effected in Europe reached America and prompted Benjamin Franklin to experiment with electricity as a therapeutic measure, and he related his experiences to a friend in this manner: "People were brought to me from Pennsylvania and the neighboring provinces to be electrified; which I did for them at their request. My method was to place the patient in a chair and draw a large number of sparks from all parts of the affected limb or limbs. Then I fully charged six two-gallon jars, each of which had about three square feet of surface coated; and I sent the united shock through the affected limb or limbs; repeating the shock commonly three times each day." Franklin noted temporary improvements, but the general result of his attempt to utilize electricity for curative purposes seems to have coincided with the experience in Europe of the Abbé Nollet, who said he did not know of a permanent cure by electrification.

Galvani's observation that the limbs of a freshly killed frog were thrown into violent convulsions when placed close to the prime conductor of a frictional electric machine led to much physiological experimentation, first upon invertebrates and later on warm-blooded animals. These experiments supplied much valuable information with reference to the various forms of response to electric stimulation, and proved that both the voluntary and involuntary muscles were affected.

At the beginning of the 19th century galvanic electricity was in use by physicians as a therapeutic measure particularly for the treatment of those diseases

which had been found to receive benefit from frictional electricity. Amateur investigators were proclaiming galvanic electricity as a specific for all kinds of nervous disorders and paralytic affections, deafness, blindness, suffocation, etc. These unwarranted and unauthorized claims soon brought electrotherapy into such disrepute that the use of electricity as a therapeutic agent was temporarily discontinued.

Modern electrotherapy dates only from 1847 when a French physician, Dr. G. B. A. Duchenne, discovered that individual muscles could be stimulated by the application of electrodes to the overlying skin. Before this the general twitchings produced by an electric shock had been observed, but, as at that time all impairments of movements were included under the term "paralysis" the pathology of which was unknown, very little progress had been made in the way of specific electrotherapy. Duchenne now devoted his attention to specific treatment, choosing as his subjects the class of incurable paralytic patients in the large hospitals of Paris. He employed induced currents, and his success in restoring health to these sufferers was so great that it gave the special impulse which resulted in the formation of a practical specialty of electrotherapeutics. Other men such as Remak, vonZiemssen, Erb, Addison, Crusell, Gull, Bird and Benedikt assisted in the modernization of electrotherapy, and widely extended the usefulness of electricity as a diagnostic and therapeutic agent.

The general benefits which are derived from electricity are well known. The benefits which have come to medicine are not so familiar, but these, too, are so numerous that we can only skim the surface with the statement that the development of a method of measuring dosage, the discovery of X-rays, and the standardization of electrical apparatus for the purpose of diagnosis and treatment have brought about a true appreciation of electrotherapeutics. All forms of electric current are now used in the treatment of disease, the kind of current and the way in which it is applied depending on the result to be effected, and the usefulness of electricity seems all the more wonderful when we consider that most of the cases successfully treated are those for whom there seems no further hope by other methods.

If the placing in the hands of physicians of a curative agent for the relief of conditions which could not be helped by other remedial measures were the only benefit which had come to medical science, it would be amply repaid for the part it has taken in the development of electrical science. It has received, however, an equal benefit in a diagnostic way, for what could be more wonderful than the X-ray machine which makes it possible to examine the "inside" of a patient; the electrocardiograph which graphically records the action of the heart muscle; the bronchoscope for inspecting the interior of the bronchial tubes; and the electrostethoscope by which the heart sounds can be intensified and heard for a considerable distance, not to mention the numberless other practical uses in medicine.

When Franklin was asked what use there was in his electrical experiments he replied by asking: "What is the use of a baby?" When Faraday was similarly questioned he responded that he was endeavoring to make electricity useful. Franklin realized that electrical science was a very promising infant, and Faraday knew that the child must be put to work to overcome complaints such as the follow-

ing made in the year 1840: "It must be allowed, that the case has not been the same with electricity as with magnetism. The latter, by the invention of the magnetic needle, has served to render navigation more secure, and to discover the new world, a source of new riches, new wants and of new evils to the old one. But electricity has not yet produced anything of so much importance, to mankind, and to the arts, if we except the analogy now proved between the electric fire and lightning; an analogy which has given rise to a pretty sure preservative from the effects of that dreadful meteor; for in regard to the cures effected by electricity, it must be acknowledged that they are either rare, or not well ascertained."

Only a century has elapsed since the discoveries of Faraday and Henry introduced the modern era of electricity, and since Duchenne laid the foundation for present-day electrotherapy, but this short period of time has been sufficient to overcome all complaints concerning the uselessness of electricity. The electrical inventions have come with such clock-like regularity that it would seem that they have been timed to keep interest in the subject alive, for as soon as the novelty of one invention waned another of even greater significance would be made to encourage the workers on to further effort.

This review, which has purposely been made brief and consequently incomplete, including only a few of the items of great importance in the early stages of electrical development most likely to be overlooked by the present generation, calls to mind what great good can come from seemingly trivial experiments in the field of pure science.

With the thought of the times focused on the matter of devising new methods of utilizing the universal servant, electricity, undoubtedly what we now regard as modern phases will before long be classed among the early ideas and undertakings of electrical science. So while lauding, as we should, each new advance, let us occasionally call to mind that pharmacists and physicians, by fundamental contributions, helped to make electrical accomplishments and achievements possible.

BARBITURATES: ALLEGED DANGERS.*

Gillespie (Guy's Hosp.) contributes an exhaustive and reasoned article in defense of the barbiturates. The article does not lend itself to abstraction, but a few points may be mentioned. A review of the published records to the end of 1932 fails to show a case in which these drugs, in single or repeated therapeutic doses, have caused death in the absence of complicating factors. In complicated cases (with one possible exception) the drug has never been the essential cause of death. The margin of safety (the ratio of customary maximum dose to minimum recorded lethal dose) is with barbitone 1:5, and with phenobarbitone 1:3; with the newer barbiturates data are not sufficient to permit such a calculation. Idiosyncrasy has to be reckoned with in a proportion of cases—about 3 per cent or less, but this is chiefly a matter of skin conditions or neurological disturbances: there is no case on record of a single therapeutic dose, even in an idiosyncratic patient, having a lethal effect. Contraindications, or indications for caution, are: (1) old age (smaller dose); (*a*) kidney disease, absolute except in pernocton or nembutal, which are contraindicated in (3) liver diseases; (4) advanced heart or lung disease (smaller doses and not continued); (5) toxæmia (sepsis or possibly hypothyroidism); (6) idiosyncrasy, to be borne in mind on first administration. Addiction may occur, but is unlikely, as the barbiturates do not afford the same euphoria as alcohol or morphine, while their withdrawal is not accompanied by the same distressing results.

* R. D. Gillespie, "On the Alleged Dangers of the Barbiturates," *Lancet* (February 17, 1934), 337–345.

ANTOINE JEROME BALARD, PHARMACIST AND CHEMIST.*

BY JOHN E. KRAMER.

In perusing the history of science we find in bold letters the names of many great men, workers in this field whose accomplishments have won for them great renown. Yet, here and there, we see a name not so familiar, but still deserving more attention than has been accorded. Let us take, for example, the case of Antoine Joseph Balard, French pharmacist and chemist, born in Montpellier, France, September 30, 1802. His education was laid along the lines of pharmaceutical training and was acquired under the Faculty of Sciences of his native town. His teaching ability, however, was so pronounced that he soon became chemistry assistant, and later professor of Chemistry at the Royal College, the School of Pharmacy and the Faculty of Sciences at Montpellier.

Balard qualified as a pharmacist and established himself in business. What spare time he had after the demands of his professions had been met was spent in the work he liked best, chemical research. The scene of his activities, Montpellier, is situated on the Mediterranean Sea, and a nearby salt marsh provided material for much investigation. Certain startling reactions aroused his suspicions and after much intense work he came upon a substance which he ascertained to be a previously unknown element.

Because of its odor, when its fumes came in contact with the air, the element was named bromine, after the Greek word "bromos" meaning stench. The name, however, was bestowed upon the substance by the famous Gay-Lussac, after Balard had called it muride, from the world "muria," meaning brine. Needless to say, Gay-Lussac's appellation remains to this day as the proper one.

It is interesting to note that another famous man of that day, Liebig, had his hand, or rather, didn't have his hand in the early days of bromine. Some years before the discovery Liebig had been sent, for assay, as an unknown, some nearly pure bromine which had been obtained as a by-product in the manufacture of salt. He laid it aside, thinking it some other substance and, when bromine was announced, immediately placed his sample in his "Cupboard of Mistakes" to constantly remind him of his lost opportunity to be the discoverer of a new element.

Balard was only 24 years old when he came upon bromine, in 1826, and his reputation and fame from this discovery were instrumental in his election to the chair of Chemistry in the Faculty of Sciences in Paris, succeeding L. J. Thenard, French pharmacist and chemist, famous for his discovery of hydrogen peroxide. In 1844 he became a member of the Academy of Science and in 1851 he was appointed Professor of Chemistry in the College of France. In this latter eminent position he had the famous Berthelot as a student, then as assistant and later as a colleague.

The sea water which furnished him his clues for the discovery of bromine also induced him to devote much time to the problem of extracting soda and potash from the briny deep. Fate was cruel in this instance, for just as he had mastered the problem, rich deposits of the substances he sought were found in the Stassfurt district. He also conducted much research on bleaching compounds of chlorine,

* Section on Historical Pharmacy, A. PH. A., Washington meeting, 1934.

and was the first to advance the theory that bleaching powder is a double compound of calcium chloride and hypochlorite.

Organic chemistry provided another field of investigation for Balard and we find records of his papers on the decomposition of ammonium oxalate, forming oxamic acid, papers on amyl alcohol, cyanides and the difference in composition between nitric and sulphuric ethers. He was a frequent contributor to the "Annales de Chimie et de Physique."

In 1868 he was made Inspector General of Superior Instruction in France and on March 30, 1876, his death occurred in the city of Paris.

ANTOINE JEROME BALARD.

Let us take a look at Balard's character, for his attitude toward life and work was responsible for a great forward step in the advancement of Science. It seems that this pharmacist-chemist, who had brought fame to himself in the discovery of bromine, was more or less content to ease along on the strength of what he had done. With the praise that was bestowed upon him, he might have reacted in one of two ways. He might have become conceited and overbearing or he might have been fired with the great ambition to find new worlds to conquer. But, instead, he chose the middle path, continuing in his unperturbed, even manner to perform his experiments in the back room of his pharmacy, or else, as was his wont, wander around to the laboratories of his friends, seeing what they were doing, listening to their plans and making suggestions from his own wealth of information. Goodness knows how many of his casual suggestions were put to work to the glory and fame of the user.

However, we do know of one such instance. Louis Pasteur, whose discoveries and works are so well known and so beneficial to us all, was in the midst of his efforts to solve the very perplexing problem of where microbes came from. Some of the scientists of the day were backing the spontaneous generation theory, but Pasteur was of the idea that they came from the air, and were wafted by the air, on dust particles, to all the places where microbes were found. Pasteur found his theory hard to prove, for, try as he might, he could not get his yeast mixtures, the medium of microbe cultivation that he used, dust free. Every time he heated his flasks, dust-laden air would rush in and in a short time the microbes could be seen increased manifold. Pasteur was up against a blank wall when Balard strolled in, heard the story, summed up the situation and rather nonchalantly suggested that Pasteur draw the necks of his flasks into the shape of an "S" lying on its side, patterned after the neck of a swan busily engaged in picking some article from the surface of the water. The suggestion made, Balard continued on his visitation rounds, and re-

turned some time later to have Pasteur excitedly tell him of the success of the experiment. Air had come back into the flasks through these queer shaped necks but no microbes had developed. The germ-laden dust had been unable to go up through the up-turn of the horizontal "S."

But proof was still necessary, so Balard suggested that Pasteur shake his flasks so that some of the culture medium wash through the entire neck and then return to the main body of the flask. Once more Balard sauntered out of the great man's laboratory, and once more Pasteur feverishly followed his advice. Just as Balard had contended, the necks of the flasks gave up enough microbes to make the yeast soup swarm with newer generations in a very short time. The spontaneous generation theory was shattered, and Pasteur was credited with the entire task. De Kruif, in his "Microbe Hunters," describes Balard's nature very admirably in just one sentence. Telling of a brilliant meeting of great scientists at which time Pasteur did his very efficient theory-exploding, the author said, "If Balard was there, you may be sure he applauded as enthusiastically as the rest. A rare soul was Balard."

Although we find the preceding paragraph to be surprisingly true, Pasteur was deeply grateful to Balard for past favors done. Balard had been one of Pasteur's teachers and personal advisers, and had been instrumental in obtaining Pasteur's connections with various investigations and with certain institutions. That he was appreciative is shown when the position of Inspector General of Higher Education was left vacant. Pasteur was immediately proposed for the post but at the same time Balard put in his application, whereupon Pasteur made this gracious gesture in writing, "Your Excellency must know that twenty years ago, when I left the École Normale, I was made a curator, thanks to M. Balard, who was then a professor at the École Normale. A grateful pupil cannot enter into competition with a revered master, especially for a post where considerations of age and experience should have great weight." Balard, consequently, received the position.

Unambitious and indolent, rather given to watching others than doing his own work, Balard was content to let life take its course and human events pass their way unhampered by any more interference from him. He is not as well remembered as others he taught in his school, helped in their laboratories and probably served in the capacity of a pharmacist, and who have received the recognition of time and history and remain forever in the minds of men.

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PHILADELPHIA COLLEGE OF PHARMACY AND SCIENCE.

The formation of State Associations was but the beginning of the work which the AMERICAN PHARMACEUTICAL ASSOCIATION has done to touch the life and the individual pharmacist and the health of the public.

THE DEPARTMENT OF THE AMERICAN ASSOCIATION OF COLLEGES OF PHARMACY

C. B. JORDAN—CHAIRMAN OF EXECUTIVE COMMITTEE, A. A. C. P., EDITOR OF THIS DEPARTMENT.

Editor's Note: The following paper on 'Effect of NRA Codes on Retail Trade' by an economist as well known as Mr. Wroe Alderson is sure to command attention. Your Editor can only urge that it be read with thoughtful care.—C. B. JORDAN, *Editor*.

EFFECT OF NRA CODES ON RETAIL TRADE.

BY WROE ALDERSON.

In considering the broad problem of the effect of NRA codes on retail trade there are five major aspects of the problem which may be considered. These are:

The volume of retail business done
The morale of retailers and their support of the Recovery Program
The competitive position of classes of retailers
The bargaining position of retailers and their suppliers
The efficiency of retail distribution.

In so far as the activity of retail trade might be increased by the Recovery Program, it would mean nothing more, of course, than a reflection of the improvement in business as a whole. This is aside from such general considerations as the relative improvement in consumer goods industries and capital goods industries. Looked upon as a symptom of recovery, the volume of retail trade has not shown a particularly encouraging trend.

The Bureau of Foreign and Domestic Commerce has been compiling several series to indicate the trend of retail trade for several lines. Reports now available for the first three months of this year show a general increase in volume of retail business over the same three months of last year. This is particularly marked in what is called the Rural Store Index. This increase may result from the payments that have been made to various classes of farmers under the Agricultural Adjustment Program and to various other disbursements of relief funds in the rural areas. The second greatest increase is in the case of automobiles. The indications here point to a really fundamental increase in wide-spread purchasing among persons of moderate means. Number of units purchased has increased much more than total volume of sales, indicating that a trend toward the more popular priced car. At the same time automobile financing has increased more than either units or volume, which will undoubtedly be characteristic of an increase in automobile purchase among classes of moderate income.

In other lines covered increases in value have been more than offset by increases in the retail price level. In other words, there has apparently been fewer physical units of goods sold at retail rather than a greater number. This may not mean that the total consumption of goods has actually been less since the various relief agencies have not used the existing channels of distribution in handling all commodities distributed on a relief basis.

One of the most unfortunate consequences of NRA has been its effect on the morale of retail trade. The National Recovery Administration began its work last summer in a way that indicated that it was not conscious of the importance or perhaps even of the existence of retail trade. The first several months of policy development were based entirely on considerations of the problems of the manufacturer, particularly in the heavy industries. The Administration came sharply up against the problem of retail trade when the Blue Eagle campaign was instituted. General Johnson had been impatient with the progress attained on manufacturing codes but the Blue Eagle instead of accomplishing the results desired in that direction, involved him inextricably with considerations of retail distribution.

One of the biggest aspects of the general problem of the effect of NRA on retail trade is thus the political problem of the effect upon the morale of retailers and through them upon public support of the Recovery Program arising from the peculiar way in which retailers came into the picture. Having first been told both in print and in conversations with their representatives who came to Washington that the program was not primarily interested in the retailer and might overlook him entirely, the retailer, because of his direct contact with the consumer, might have been the agent for selling the whole program solidly to the entire country if he had been handled with more consideration.

The policy originally announced of leaving considerations of retail trade for treatment at a much later date was probably a sound one. It would have been a much easier problem to secure full compliance and strict enforcement against violators if only the larger manufacturing industries had been covered. Securing compliance among retailers could naturally be expected to be a slow process because of the great number of small and sometimes irresponsible individuals engaged in the retail business. Retail violations are likely to be well known in the community and widely discussed because the retailers' operations are so open to public inspection.

From the standpoint of creating employment opportunities, the NRA could not perhaps afford to overlook retail trade with almost as many millions of people employed as manufacturing industries. It can be stated with certainty, however, that these facts did not occur to the leading minds in the NRA until much later and as a matter of fact, the retail codes were never handled in such a way as to capitalize to any great extent the employment possibilities offered. Ironically enough, the greatest single potential field for real employment was brought into the picture more or less accidentally through a failure to visualize the way in which the so-called Blue Eagle campaign would immediately become involved with retailing.

Effect of NRA on the competitive position of classes of retailers is one of the most interesting aspects of NRA and its consequences. Various groups of competing business men have become highly specialized in the degree to which they make use of various competitive devices. In the retail field three of the leading types of stores from the standpoint of competitive position have been limited price stores, cut price stores and service stores. There are other lines of cleavage such as small and large stores, specialized and general stores and groups distinguished by particular method of operation such as the chain store and the mail order house.

The line of division indicated in the first instance is the one which has been brought most sharply into the foreground by the attempt to set up NRA codes. Some of the most vital code provisions carried threats of upsetting completely the

competitive equilibrium in retailing because these code provisions seemed likely to affect the position of one class of retailers more drastically than that of another class of retailers. The limited price stores had made a place for themselves on the basis of fixed and well-known prices for a variety of items such as 10¢ for a tack hammer or $5.55 for a pair of shoes. These stores had flourished during the past several years of declining wholesale prices. Their greatest concern related to the possibility of drastic increases in the cost of labor which would make it impossible for them to maintain their present fixed price lines which were the principal basis of their merchandising appeal to the public. One result of their having been so deeply perturbed over these matters was the formation of two brand new trade associations which called into their services two of the shrewdest merchandising men in the country. These were Dr. Paul Nystrom for the limited price variety stores and William Girdner for the fixed price chain shoe stores. Up to the present this group has come off fairly well since the increase in labor cost was much less than they had feared it might be. Some variety chains reported national improvement in their position as a result of the enforced wage increase. They found that they were getting a better class of help at a higher minimum wage and that these employees were bringing courtesy and intelligent sales effort into the variety store operation for the first time.

The service type of store was most concerned about the other step in the program for benefiting labor, namely, the shortening of hours, particularly as it implied or might require the shortening of store hours. The downtown stores generally would have had their competitive positions somewhat improved in relation to the small neighborhood stores if there had been a drastic cut in the number of store hours permitted. Many of these small merchants obtain a considerable portion of their total business solely because they are able to remain open for a longer number of hours than the larger store. Here again the tendency of the NRA to deal gently with retailing so far as prescribing a new labor burden was concerned kept this second group of retail stores from suffering any loss of competitive efficiency in the direction which they particularly feared. It would be very interesting to know just what was the basis of the very lenient policy concerning labor requirements in retail codes since some of those who were frankly representing the interests of the retailer at hearings admitted openly to administrative officials that their group was not being asked to carry their fair share of the recovery load but without apparently having any effect on the administrative attitude.

The third class of stores were those whose volume depended largely on price appeal. This included stores which had to offer prices to attract customers because of downtown locations and stores which were using aggressive price cutting in an effort to make a place for themselves as newcomers to the field during the course of the depression. This group included chain stores, department stores, the pine board store in the drug field and the supermarkets in the grocery field. All of these types devoted the closest attention to any proposed clauses which were designed to create price appeal by prohibiting sales below purchase cost or some other predetermined level.

The result in this direction has been to favor the moderate price cutter as against either the drastic price cutter or the store depending on service appeals. While some price protection has been given in the Codes, it is sufficiently moderate

to permit the department store and chain store to sell certain items at prices lower than would normally be offered by the small service retailer. The pine boards and supermarkets are barred under the Code from exerting the full force of price cutting which they have used in the past. The general effect, therefore, is to restore the general status of competition as far as price appeal is concerned, which existed prior to the depression.

The earnings of retailers depend in part on the day to day outcome of the constant struggle between the retailer and his supplier for the larger share of the amount paid by the consumer to cover the functions performed by both. The activities of the NRA have thrown the balance slightly in favor of the supplier, particularly in the case of small manufacturers supplying the department stores. Here again this could be viewed either as an interference with the present competitive equilibrium or a return to the relative status prior to the depression. Over a long period the present policies of NRA would work more and more against the retailers as compared with the supplier. There is always, of course, the definite possibility that present policies would be modified before they had led to any drastic upsetting of the present balance of power between retailer and supplier.

From the standpoint of the general public interest, the most important question of all is what effect a Recovery Program may have on the total cost of distribution. It has long been held by many people that one of the greatest needs of our economic system was to be able to perform at lower cost the function of transferring goods from the hands of the manufacturer to those of the consumer. Specifically in connection with the Recovery Program several of the Recovery Agencies and particularly the A. A. A. have placed major stress on reduction of the cost of distribution as one of the fundamental objectives of the program. This must be acknowledged as a vital problem and one that must be solved for purposes of long range reconstruction even though its bearing on immediate recovery may be more limited.

While such a cost reduction is certainly to be desired, the important question is where to take hold of the problem since it can be shown beyond the question of a doubt that many of the efforts to reduce the cost of distribution have actually tended to increase costs. This is sometimes true for example, in the case of individual manufacturers who feel that the cost of the wholesale function as performed by the independent wholesaler is too high to attempt to sell their merchandise directly to the retailer. Only too often the manufacturer finds that he is not able to do the job as cheaply as the wholesaler. He may still hang on to the wholesale facilities which he has established either because it is difficult to withdraw his investment in them or because he finds some compensating advantage in an increased ability to control his market even though the function is performed at a higher cost.

So far as administrative points of view are concerned, the most persistent and fallacious bit of thinking concerning distribution cost has been the assumption that the small retailer was necessarily inefficient because he was small and that he should therefore be eliminated or his numbers greatly reduced. To the extent that this point of view is allowed to determine policies, the efforts of reducing the cost of distribution may have an effect opposite to that desired. As opposed to this point of view the following things can be definitely shown:

1. That the optimum size of unit in retailing is at a very moderate volume point in most lines of trade.

2. That the advantages of aggregating individual units into chain systems are advantages which can be duplicated by coöperative effort between small retailers and is not inherent in the corporate form of organization or outstanding excellences of chain management.

3. That the function of service retailing cannot be fairly judged except in relation to a definite measure of how much service the consumer wants. Retailers create place utility and it is obvious that the cost of creating it will be high if the consumer demands that commodities be brought within a few blocks of his home.

4. That the really inefficient small retailers make up a very small fraction of the total volume and that the consumer does not ordinarily carry an additional load because of their presence in the picture since the greater part of the loss which such retailers sustain through excessive operation costs is in the form of wasting their own assets.

5. That the small retailer is in several lines engaged in subsidizing the expensive fringe of retail distribution and that a unified system which attempted to cover the market completely might find its average cost considerably increased by the necessity for maintaining distribution at the points where such small retailers now maintain it.

Gould's "Pocket Pronouncing Medical Dictionary," 10th edition. P. Blakiston's Son & Co., Inc., Philadelphia. Price $2.00, plain; $2.50, with thumb index. Flexible cover, 4 x 6½ inches. Contains over 40,000 words, giving the pronunciation and definition of the principal words used in medicine and the collateral sciences, including illustrations of the arteries, muscles, nerves, bacteria, bacilli, micrococci, spirilla, etc.; thermometric scales, revised dose list of drugs and their incompatibilities, systems of weights and measures, based upon U. S. Pharmacopœia X and revised veterinary dose tables. By George M. Gould.

In selecting the new words care has been taken to include those of sound and permanent value. Twelve pages are given to symbols and abbreviations. The definitions are brief but definite. "The Physician's Dose Table" has been prepared by Wilbur L. Scoville; included therein the names of Remedies are given in the first column and, in sequence, Doses in Apothecaries System, Metric, Solubility, Important Incompatibilities. The Veterinary Dose Table was prepared by Dr. W. S. Devoe, formerly inspector of Animal Industry, U. S. Department of Agriculture and revised by Dr. V. G. Kimball, assistant professor of Veterinary Medicine, University of Pennsylvania. The value of a dictionary is best determined by the users, and the revisions and large sale have evidenced the approval of the practitioners of medicine and others who have the volume in their libraries.

Pharmaceutical Formulas (P. F. Vol. II) published 1934, supplementary to Vol. I, and known as "The Chemists' Recipe Book." Contains formulas for adhesives, beverages, cleaning materials, culinary and household requisites, horticultural and agricultural preparations, inks, lozenges, perfumes, photographic preparations, polishes, soaps, toilet articles, varnishes, veterinary preparations, etc., including numerous descriptions of practical methods employed in their manufacture, and other information of use to pharmacists and manufacturers. Over 1000 pages. Price by post, 15 shillings 6 pence.

The formulas are to a large extent representative of the "correspondence columns" of the *Chemist and Druggist;* the replies to correspondents have been arranged under various headings and the publishers advise that, as far as possible, the formulas have been checked by experiment. Formulas from foreign official and non-official publications (other than British) are included and, in this connection, it may be pointed out that strengths of preparations and composition of them may vary, this should be taken into consideration in compounding; also quantities of this book, unless expressed in the Metric System, or otherwise stated, are given in British units of weights and measures. The *Chemist and Druggist* is well and favorably known to pharmacists and speaks for the value of the Book herein noted.

THE CONFERENCE OF PHARMACEUTICAL LAW ENFORCEMENT OFFICIALS

MINUTES OF THE SESSIONS HELD IN SHOREHAM HOTEL, WASHINGTON, D. C., MAY 10 AND 11, 1934.

The sixth annual meeting of the Conference of Pharmaceutical Law Enforcement Officials was convened by Chairman R. L. Swain at 9:30 A.M. in the Card Room, with the following present: Messrs. J. W. Slocum, W. F. Mead, Iowa; R. C. Reese, W. Mac Childs, Kansas; Hugo Schaefer, George W. Mather, F. C. A. Schaefer, C. P. Wimmer, New York; Robert C. Wilson, W. S. Elkins, Georgia; A. L. I. Winne, Virginia; J. Lester Hayman, G. O. Young, West Virginia; C. T. Gilbert, Connecticut; Joseph Burniak, Michigan; J. B. Pilchard, L. L. Walton, R. R. Gaw, Pennsylvania; N. N. Brakke, North Dakota; Rowland Jones, South Dakota; C. S. Pierce, B. K. Murdock, L. H. Marr, Maine; W. C. Muesing, J. P. Jellinek, Minnesota; Henry F. Hein, Texas; P. R. Loveland, New Jersey; W. Bruce Philip, J. W. Lee, A. C. Taylor, R. A. Veitch, Washington, D. C.; F. V. McCullough, Indiana; Frank C. Purdum, W. F. Reindollar, R. L. Swain, Miss B. Olive Cole, Maryland; M. N. Ford, Ohio.

Chairman Swain made a verbal address and then called for the report of the Secretary-Treasurer.

THE REPORT OF SECRETARY-TREASURER.

BY M. N. FORD.

Since the last annual meeting of the Conference, the Secretary has had considerable requests from different states for information which was promptly furnished. There being no particular court decisions furnished the Secretary, there have been no bulletins sent out since the last meeting. Proceedings of the last annual meeting were published in the JOURNAL and it has been recommended by the Chairman that reprints be secured and made available to the Conference members as soon as possible.

There have been no expenditures of money since our last annual meeting, therefore, we have on hand a balance from the last meeting of $170.67. We have received from Chairman F. C. A. Schaefer, of the Finance Committee, $110.00, therefore, we have on hand at this time $280.67.

Upon motion of Mr. Winne, seconded by Mr. Jones, the report of the Secretary-Treasurer was approved.

The Conference also approved obtaining reprints of the proceedings of the last annual meeting and that they be made available to the members as soon as possible.

REPORT OF FINANCE COMMITTEE.

The Finance Committee appointed by Chairman Swain, sent out an appeal to the Boards of Pharmacy for contributions of ten dollars for the Conference. This Committee, not having been appointed until recently, did not have ample time to get many replies from their appeal; however, the Committee did receive $10.00 contributions from the states of Maryland, Ohio, Kentucky, Connecticut, North Carolina, North Dakota, New Jersey, West Virginia, Arkansas and Wisconsin, and $5.00 contributions from the Board of Pharmacy of Pennsylvania and from the West Virginia State Pharmaceutical Association, making a total of $110.00. The Committee has had favorable replies from other states who will forward their contributions a little later.

ROWLAND JONES
W. MAC CHILDS
WM. HANKINS
HUGO SCHAEFER
F. C. A. SCHAEFER, *Chairman.*

Upon motion by Mr. Mead, seconded by Mr. Gilbert, the report of the Committee was approved.

A question was raised as to the legality of the fee being paid by the Board of Pharmacy and a discussion was entered into by Messrs. Wilson, Childs, Winne, Mead and Hayman.

At this time Chairman Swain introduced the **Hon. Herbert Levy** of the Maryland Bar who addressed the Conference on the subject of "The Place of the Attorney-General in the Legislative and Law Enforcement Program." Mr. Levy spoke, in part, as follows:

Some of you may recall that I spoke to this group at its meeting in Baltimore some two or three years ago. Since that time, laws have been enacted with such bewildering rapidity and of such sweeping effect that an examination of the rôle of the Attorney-General brings to light new possibilities of useful service on the part of the person holding that office. In general it should be said that the place of the Attorney-General is traditionally at the head of the law enforcement division of government; whereas on the other hand he has no place traditionally in the legislative program.

The Attorney-General of the United States has the duty of representing the government in law suits in the Supreme Court and in the Court of Claims; and in addition is head of the Department of Justice, having as such, as Bryce has remarked in his analysis of the American Commonwealth, powers comparable to those of a minister of justice in a European cabinet. Further, the Attorney-General has the important duty of advising the President and the heads of executive departments by opinions on questions of law submitted to him. Significant is the inability of the Attorney-General to render opinions to either of the houses of Congress and equally so is the limitation whereby the Attorney-General cannot give opinions except upon questions actually arising in the department requesting the opinions. Finally, the Attorney-General may at times act as draughtsman of legislation to be proposed in Congress.

The actual duty of prosecuting offenders against the federal laws is not performed unless and until the appellate courts are reached. But the connection between the district attorneys and the Attorney-General gives the Attorney-General contact with and responsibility for the prosecution of offenders even in the lower courts. The duties of the various State Attorneys-General vary in each state.

A contrast between the United States Attorney-General and the Attorney-General of Maryland, as an example, may be found in the fact that the local States' Attorneys are not subject to the control of the Attorney-General of the state who can only participate in a prosecution in a lower court when required by the Governor or the General Assembly to aid the States' Attorneys.

In summary, therefore, of the place of the Attorney-General in the law enforcement program, it may be said the United States Attorney-General occupies through the district attorneys a most responsible position in this regard whereas the State Attorney-General holds one of much less importance.

In the rendering of opinions there is also some contrast to be noted. In Maryland, for example, the Attorney-General may render opinions when required to do so either by the General Assembly or by one of its houses.

The rendering of opinions and the analogous duty of drawing proposed legislation may be described as functions midway between law enforcing and actual "legislating." A strict construction of existing statutes may for example directly bring about the passage of supplementary acts by the legislature. A liberal construction may bring about restrictive legislation by the law-making body. Or the injection of some personal point of view in a law being framed for a governmental department may directly affect legislation.

The very possibility of influencing the character of legislation by either of these methods raises the interesting question of the separation of powers. Needless to say any attempt on the part of the Attorney-General directly to color legislative changes through the use of his services by those charged with legislative duties, presents the same problem in a form in which the separation of the governmental powers can be studied as more strikingly productive of good or evil. The actual proposing and advocating of particular legislation by an attorney-general is so unusual, and so unlikely, because of the resentment it would cause to legislators, that it need only be regarded as the extreme to which this particular combination of governmental functions may ever proceed.

"Separation of Powers" is a phrase familiar to even the most casual student of civics who has heard from school-boy days of the division of the government into executive, legislative and judicial parts. The origin of the phrase appears to go back to the "Spirit of Laws" written by the French nobleman Montesquieu in the middle of the Eighteenth Century. It has been said of this

versatile writer (whose "Persian Letters" are known to many not the least interested in government) that his gift of generalization was so happy that from a mass of incomplete or even totally inaccurate information he could extract a principle of the widest application. With his other great gift of forceful and epigrammatic expression he could then express the principle in terms of terse lucidity.

At the time when he was writing, the Hanoverian monarchs of England had been on the throne only a few years. And the cabinet system of government, made necessary by their inability to speak English and their ignorance of English affairs, to say nothing of their frequent absences on visits to their German kingdom, was only slightly known to Europeans. But the division of the government already definitely marked was not lost on Montesquieu when he analyzed the British constitution. It is in this analysis that he uses the phrase "Separation of Powers." And he there says:

> "When the legislative and executive powers are united in the same person or in the same body of magistrates, there can be no liberty."

The idea had already come to America and was embodied in most of the state constitutions at the time of the drawing of the Federal constitution. But the words of Montesquieu, quoted by Madison in the *Federalist*, kept the principle clear in the minds of the members of the constitutional convention.

It may be appropriate to notice that Madison particularly comments upon the force of the statement of the principle in Article 8 of the Maryland Declaration of Rights:

> "That the Legislative, Executive and Judicial powers of Government ought to be forever separate and distinct from each other; and no person exercising the functions of one of said Departments shall assume or discharge the duties of any other."

Interesting as may be the study of the origin of the idea it is still more interesting to observe with what force the principle has been adhered to through all the successive changes both in Federal and state forms of government.

Applied to the activities of the Attorney-General as a member of the executive department of the government it obviously prevents his voting in any legislative body, as does the Attorney-General of England, who is a member of Parliament. It also prevents any close official connection with the law-making power.

His problem is not to influence the legislature. I learned from practical experience that legislators are very jealous of their prerogatives. A wise Attorney-General should never show too much zeal in advocating departmental legislation; for immediately he does so, he is suspected of attempting to encroach upon the legislative domain.

He should thoroughly familiarize himself with the governmental problems to be dealt with so that, if called upon, he can draft the laws in clear and succinct language and then present to such as may inquire the explanations and reasons for the law. Beyond this he cannot go except at the peril of his offiial client's cause.

That does not mean his legislative activities are of no value in influencing the passage or defeat of legislation in which his official clients are interested. On the contrary, a dignified, semi-judicial presentation of the arguments in favor of the department's position usually carries considerably more weight than an argument to like effect made directly by the official involved.

Those of you who must resort to legislatures in connection with your work, take heed.

Use your Attorney-General. He can be of great help to you in the presentation of your case, but do not make too much use of him.

In other words, enforcement work, like every other kind of work in life must be administered with common sense and the Attorney-General can be of great help if you take his nose out of the law books and fully familiarize him with your problem from a practical point of view.

The lofty impartiality of the Attorney-General, who best fulfils his duties, derived as it is from principles long studied and understood finds no more useful function than in connection with the governmental changes of to-day.

Acting because of the critical condition of the country in the spring of 1933 Congress passed a series of extraordinary measures producing the most wide-spread effects, yet short and simple in

their language. The most frequently discussed of these are the NRA; and the AAA. The power which these acts placed in the hands of individuals is almost incredible. The ability of individuals to vary the meaning of the law by executive orders has given practically law-making power to executives charged with the administration of these and numerous other acts. A committee on administrative law appointed by the American Bar Association says in its report, "To a greater extent than ever before, the lawyer must look to the President's executive orders and to the releases and announcements of the several administrative agencies for accurate and up-to-date knowledge of the existing state of the law."

With no disposition whatever to criticize the bold and comprehensive program of President Roosevelt which has breathed life into an industrial civilization previously believed by many to be dying, and has truly replaced the despair of almost an entire world with hope, it seems the effect of concentration of power in administrative officials is bound to tend at least to a desire for increased power on the part of state and Federal officials generally.

The proposed Copeland-Tugwell Bill, with which, I believe, you gentlemen have some familiarity, is drawn with the highest purposes in mind: to protect the public health. But here, too, extraordinary powers are proposed to be given to individuals.

The Secretary of State may promulgate regulations governing conditions of manufacture, processing or packing, and he may in effect close a factory and then decide whether his action was justified. Meanwhile at all times any officer or employee duly designated by the Secretary shall have access to inspect any factory of the group described.

It is apparent that interpretations of this Act, which determine its ultimate scope, will vitally affect the thousands of manufacturers subject to its terms. The many questions which will arise in the minds of the army of enforcing officials will call for opinions from the Attorney-General's office, which will react upon every member of the pharmaceutical profession. Wise opinions by an Attorney-General, aware of the problems sought to be solved by the Bill, and not attempting to extend the already far-extended confines of the law, will do much to carry out the beneficent purpose of the Act while safeguarding the rights of the individual.

The Attorney-General who understands the problems of government, well serves those whom he represents by impartially giving opinions to department heads to keep them within their scope and assist them in the execution of the powers that they have been given by the legislature; and by accurately reflecting in bills prepared by him the views of the legislative officials whom he assists.

If the new type of legislation such as that recently passed, is to be permanent, the Attorney-General can do much to make the change in governmental theory less unpalatable by bringing about through his counsel and advice, tact and discretion in administration.

Following Mr. Levy's address, he submitted to questions from the Conference, after which he was given a rising vote of thanks for his splendid address.

Chairman Swain next called upon **George W. Mather,** secretary of the New York Board of Pharmacy, who presented a paper on "The Enforcement of the Poison Laws." Before submitting his paper, Mr. Mather gave a verbal report of his activities which were discussed by Messrs. Childs, Wilson, Purdum, Winne, Reese, Jones, Elkins, Gilbert, Walton and Swain.

ENFORCEMENT OF THE NEW YORK STATE POISON LAWS.

As early as 1880 the State of New York placed upon the statute books a limited type of control which surrounded the sale of medicines regarded as poisonous. This law was amended several times and in 1910 enforcement of the Pharmacy Law was placed under the Department of Education of the State of New York.

At that time the word "poison" was defined as follows:

"Poisons, where not otherwise limited, means any drugs, chemical, medicine or preparation liable to be destructive to adult human life in quantities of sixty grains or less."

The New York State Board of Pharmacy functioning under the Department was by law given the power to regulate the practice of pharmacology and to make rules approved by the Department for the supervision over the sale of drugs and medicines. In conformity with that law certain schedules known as "A" and "B" were adopted.

Schedule "A" consisted of the articles listed below: "Schedule A. Arsenic, atropine, corrosive sublimate, potassium cyanide, chloral hydrate, hydrocyanic acid, morphine, strychnine

and all other poisonous vegetable alkaloids, and their salts, oil of bitter almond containing hydrocyanic acid, opium and its preparations, except paregoric and such others as contain less than two grains of opium to the ounce."

Schedule "B" consisted of the following:

"Schedule B. Aconite, belladonna, cantharides, colchicum, conium, cotton root, digitalis, ergot, hellebore, henbane, phytolacca, strophantus, oil of savin, oil of tansy, veratrum, viride and their pharmaceutical preparations, arsenical solution, carbolic acid, chloroform, creosote, croton oil, white precipitate methyl or wood alcohol, mineral acids, oxalic acid, Paris green, salts of lead, salts of zinc or any drug, chemical or preparation which is destructive to adult human life in quantities of sixty grains or less."

Each item of medicine which was defined as poison by reason of the rule is required by law to have the name of the article and the place of the seller noted on the package or container and the label shall be printed in red ink.

Violations for infractions of the above laws are punishable as a misdemeanor and may carry a penalty ranging from $25.00 to $200.00 for each offense.

"1. 1360 Poison schedules; register. It is unlawful for any person to sell at retail or to furnish any of the poisons of schedules A and B without affixing or causing to be affixed to the bottle, box, vessel or package, a label with the name of the article and word poison distinctly shown and with the name and place of business of the seller all printed in red ink together with the name of such poisons printed or written thereupon in plain, legible characters.

"2. Wholesale dealers in drugs, medicines, pharmaceutical preparations, chemicals or poisons shall affix or cause to be affixed to every bottle, box, parcel and outer inclosure of any original package containing any of the articles of schedule A, a suitable label or brand in red ink with the word poison upon it.

"3. Register. Every person who disposes of or sells at retail or furnishes any poisons included in schedule A shall before delivering the same enter in a book kept for that purpose the date of sale, the name and address of the purchaser and the name and quantity of the poison, the purpose for which it is purchased and the name of the dispenser. The poison register must be always open for inspection by the proper authorities and must be preserved for at least five years after the last entry. He shall not deliver any of the poisons of schedules A or B until he has satisfied himself that the purchaser is aware of the poisonous character and that the poison is to be used for a legitimate purpose. The provisions of the paragraph do not apply to the dispensing of medicines or poisons on physicians' prescriptions."

The labeling of poisons also applies to proprietary remedies if they come within the scope of the rule.

Section 1354 provides as follows: "Every place in which drugs, chemicals, medicines, prescriptions or poisons are retailed, or dispensed or compounded, shall be a pharmacy, a drug store or a store; shall be under the personal supervision of a pharmacist, a druggist or a storekeeper and shall be annually registered in the month of January by the board as conducted in full compliance with law and the rules."

Prior to April 19, 1934, the control of the manufacture and sale of proprietary remedies were not within the jurisdiction of the New York Board of Pharmacy. However, on that date this section was amended placing under the supervision and control of the New York State Board of Pharmacy the manufacture and sale of articles which are poisonous.

It is anticipated that in the near future the Board of Pharmacy will formulate rules with the sanction of the Department for the control of proprietary remedies which will conform to the above amendment.

Chairman Swain next introduced **Frank C. Purdum** a member of the Maryland State Legislature, who presented a paper "Is Pharmaceutical Legislation Best Served by a Pharmacist Member of the Legislature?" as follows:

IS PHARMACEUTICAL LEGISLATION BEST SERVED BY A PHARMACIST MEMBER OF THE LEGISLATURE?

The Chairman has assigned to me a rather unusual subject. However, I think it is an important one, and am very glad to contribute what I can to this Conference of Law Enforcement

Officials. At the same time, I am aware of the fact that, unless I can tell you something you do not already know, this paper will be of very little value.

I shall cover, as briefly as possible, my outstanding experiences and impressions, particularly in connection with pharmacy, while serving as a member of the Maryland Legislature during the past eight years. I am a graduate in pharmacy; have been registered in Maryland for thirty-two years; and have been and am now, engaged in the operation of my own drug store.

The question is: Is pharmaceutical legislation best served by a pharmacist member of the legislature? This subject immediately suggests other questions. For instance, assuming for the moment that it is to the advantage of the profession to have a pharmacist in the law-making bodies, what type of pharmacist should be encouraged and sponsored by the profession to enter the field of politics? Can a clean, high class professional pharmacist seek an elective office without sacrificing some of his ideals? In what way can a pharmacist, as a member of the legislative body, be of most service to the profession of pharmacy?

The question has been raised as to whether he should take the leadership as a trained professional man, and introduce and sponsor all bills that the pharmacists may desire, be ready to boldly take the floor in opposition to all unfavorable legislation or whether he should somewhat submerge himself, and work in the background through well-selected leaders.

Obviously, this question, presenting both views of so large and important a matter, might be discussed at great length. The mere statement of the question indicates that there are advantages on both sides. Certainly, all efforts must be taken to disarm the criticism that when you, a pharmacist, introduce and sponsor legislation in the interests of pharmacy, you are largely concerned in a selfish venture. However, a discussion of what place the pharmacist should play is largely theoretical because his interest and influence are certain to become known whether he acts as a principal or as an accessory, so to speak.

As I see the whole matter, there can be no fixed rules in this respect. It depends upon the circumstances and the character of the legislation being considered. If it is of rather a technical nature such as is embraced in the adoption of experience and educational standards, or in bills dealing with specific chemical or pharmaceutical terms, undoubtedly the pharmacist should be thoroughly familiar with the subject, and be prepared to explain and answer intelligently any questions that may arise. In such a case, there is every reason why he should be the leader in favoring or opposing the measure. Here he is on solid ground, and should be regarded as the best qualified to express an expert view of all the facts involved.

If on the other hand, the legislation is more economic than technical, the pharmacist legislator may better serve by keeping in the background. This thought can be made clear by considering a bill designed to restrict the sale of household remedies to registered pharmacists. In spite of our firm belief that such a bill has a direct bearing upon public health, the average legislator is certain to regard it as a mere selfish effort to give pharmacists a monopoly of the business. In such a case, real statesmanship is demanded, and, even with the best laid plans, the thing is mighty apt to get into a snarl and possibly result in defeat, or a compromise measure just about as bad.

The pharmacist members of the legislature should seek a place upon the committee to which all health bills are referred. In Maryland, this committee is known as the Committee on Sanitation and Hygiene. I have been chairman of this committee for some years. The mere fact that I was selected for this important position carries with it the recognition that my training and experience, as a pharmacist, will have a direct bearing upon the matters which automatically are referred to this committee. Here the pharmacist sits in a strategic position. He is really on the inside. He hears both sides of the question, attends all committee hearings, may cross-examine those for or against a measure, and may present his professional and technical views to the committee. He is in position to see to it that a proper report is made by the committee, and he has all the facts should it be necessary to discuss the bill on the floor. In every instance, I strongly urge pharmacist legislators to be members of the committee to which pharmaceutical and health legislation is referred.

The right type of pharmacist can so impress himself on his colleagues that his judgment will count heavily. They begin to regard him as the best posted man in certain respects. More or less subconsciously they look to him when certain questions come up. With this, so I have found, comes a heavy responsibility. Members of the legislature have frequently told me that I should

take the responsibility in matters dealing with pharmacy and other health legislation. They feel that this is my line, and just as frankly, not theirs. Unless the matter is highly controversial, I have found a strong disposition to make me take the lead in legislation affecting the whole health field.

Recently, a bill was introduced in the State Senate, which would have granted registration as a pharmacist to one who was entitled to register in 1902, simply by filing the required affidavits, but who was not in the State at the designated period. On the surface the bill was harmless, and was designed to serve a really deserving case. However, such an act would have established a precedent which could have been, and probably would have been, very troublesome. There was no disposition to take any action on the bill until my views had been obtained. Even though I am a member of the House, the Senate wanted my views on a matter directly concerning pharmacy. I mention this incident simply to illustrate the point that a pharmacist in the legislature finds himself in position of speaking for the profession, and in a position also, to further its general standing not only in a legislative sense, but in matters dealing with its professional and technical service.

Again, when the Maryland Legislature was considering the provisions of an act to regulate the sale and distribution of alcoholic liquors, I was able to convince the body that alcohol used exclusively for the manufacture of medicinal, toilet and antiseptic preparations, flavoring extracts and other preparations unfit for beverage purposes, should not carry any state excise tax. Also that whisky and other intoxicants, when dispensed on physicians' prescriptions were medicines and thus the pharmacist should not be required to take out any State liquor license to fill such prescriptions. Let it be understood that this was not a personal victory. I was there, a pharmacist who understood the problems, and who was on the ground floor, so to speak, throughout the whole discussion.

Let me emphasize a point that is of the greatest importance. While I am fully convinced that a pharmacist as a member of the legislature can be of very great aid in furthering the legislative program of the profession, I am just as convinced that he must be given real backing by the group as a whole. I have constantly sought to have the endorsement and active support of the state associations, the board of pharmacy and other organized groups. Perhaps it would be more accurate to say that I have tried to have passed, bills which organized pharmacy has sponsored and approved. I have more nearly regarded myself simply as their spokesman.

If some dangerous, or even debatable, bill is introduced by others than our own group, having a bearing upon pharmacists, I have invariably called it to the attention of the pharmaceutical leaders in the state, and we have sat down and talked it over. The course of action that I have then followed has been in accord with the conclusion reached by the group. Up to the present, we have had no family quarrels or dissensions, and we will have none, so long as the proper men lead and so long as there is the proper team work between them and the pharmacist member of the Legislature. However, let me emphasize, it is team work that is required. If our own ranks develop opposing camps, if we once let it be known that the group cannot agree among themselves, the legislative program may as well be shelved until we can express a collective opinion and stand squarely behind it.

In conclusion, let me digress briefly into a discussion of practical politics. Legislative experience and the ability to fraternize with other members of the legislature are really great helps. Every member has a few bills in which he is especially interested. Now, I have always felt that it was wise to introduce legislation early in the session, put a real kick back of it and get it through. By so doing, you escape the pitfalls of trading and dealing once the battle is really on. Most representatives are partly or wholly controlled by district leaders or bosses as they are generally called. These bosses are not always bad and their friendship is worth cultivating. It may only cost a cigar, highball or lunch. The most successful lobbyists work through these channels. This does not show up in pharmaceutical legislation bearing upon the educational or professional sides. Invariably, however, once it becomes economic or smacking of monopoly, you will find the "big boys" want to know what it is all about.

Another thing, pharmacists as a whole do not show sufficient interest in politics. It is my belief that, in the final analysis, we get as good government as we deserve. The best citizens of any state or municipality should be sufficiently interested in politics to assure good government. The pharmacist, being both a professional and business man, has a splendid opportunity, in his

daily contact with people, to have a say as to whom his representatives should be. But is he interested? To be more explicit, we should take time to become interested in issues; we should vote in primary elections; we should seek to learn the candidate's views while he is still a candidate; in every possible way consistent with decency and civic standards, we should seek to have our voices heard and our views considered.

During recent years, any number of bills have come before the Legislature having a bearing upon public health, or upon some public health profession: Anti-vivisection bill is a regular and biennial affair; bills favorable and unfavorable to pharmacists; bills seeking to permit Christian Science or faith healers to make a charge for their services; enlarging the scope of osteopaths and chiropractors; conferring the right of optometrists to use the title "doctor;" uniform state narcotic act, these and many more have found their way to the Legislature during my terms of office.

It is my opinion, regardless of the unsavory reputation of professional politicians, that a pharmacist can serve as a member of a legislative body without compromising his character or reputation. It is my opinion, too, that a pharmacist, as a member of the Legislature, is in position to greatly advance pharmaceutical legislation. In most cases, he should take a leading, courageous and frank position. If he is the proper type of pharmacist, his views will count heavily on all matters pertaining to the pharmaceutical profession and the drug business.

P. L. Loveland of New Jersey took the place of Harry E. Bischoff on the program and spoke on the same subject as Mr. Purdum.

At this time Chairman Swain appointed the following Committee on Nominations: *Chairman*, A. L. I. Winne, Virginia; Hugo Schaeffer, New York; L. L. Walton, Pennsylvania.

The following Committee on Resolutions was appointed: *Chairman*, J. Lester Hayman, West Virginia; W. S. Elkins, Georgia; Roy Reese, Kansas.

Chairman Swain next called upon **W. Mac Childs,** secretary of the Kansas Board of Pharmacy, who made an oral address on the subject of the "Public Health Council of Kansas and the Values of Its Principles to the Pharmaceutical Program."

At 12:45 P.M. upon motion duly seconded, the Conference adjourned.

Thursday, May 10th.

At 8:00 P.M. the Conference met in joint session with the Section on Education and Legislation and Conference of Pharmaceutical Association Secretaries, in the Club Room of the Hotel Shoreham.

SECOND SESSION.

The Second Session of the Conference of Pharmaceutical Law Enforcement Officials convened at 2:30 P.M., Friday, May 11th, in the Grill Room of the Shoreham Hotel.

Chairman Swain called the meeting to order and the first order of business was the discussion to collect court decisions with the idea of raising sufficient revenue to have same printed for distribution to members of the Conference. Both Mr. Mead of Iowa and Mr. Elkins of Georgia volunteered a subscription up to twenty-five dollars each in support of such a program either through the board or association.

The next question discussed was the time of meeting of the Conference, as many of those interested in the Conference meeting would like very much to have a meeting scheduled immediately after the National Association Boards of Pharmacy conclude their sessions. The chairman and secretary were directed to use their influence to have such an arrangement made.

Chairman Swain next called upon **A. L. I. Winne** of Virginia, who presented a paper on "Report of Special Committee to Define the Terms 'Patent Medicine' and 'Proprietary Medicine,'" as follows:

REPORT OF THE COMMITTEE ON DEFINITION OF "PATENT MEDICINE" AND "PROPRIETARY MEDICINE."

Your appointed committee to report on a study of adequate definitions for the terms "Patent Medicine" and "Proprietary Medicine" is unfortunately able at this time to render but a superficial report. The chairman of the committee acquainted the membership with the purpose of the study and received an informative response from one other member. The secretaries of all State Boards of Pharmacy were communicated with and information was returned by some thirty-

eight states. Of this number, thirty states reported as having no definition for the terms "Patent Medicine" and "Proprietary Medicine," although the terms were embodied in the pharmacy laws of the respective states. Several states have attempted to have the terms defined by their Attorney-Generals and some several have court decisions with rather vague interpretations of the terms. In no instance is there a clean-cut and satisfactory definition of the terms.

The states which report as having no definitions whatever are:

Alabama	Kansas	Oregon
Arizona	Kentucky	Pennsylvania
Delaware	Montana	Rhode Island
District of Columbia	Nebraska	South Carolina
Florida	New Jersey	Tennessee
Georgia	New Mexico	Texas
Idaho	North Carolina	Vermont
Illinois	North Dakota	West Virginia
Indiana	Ohio	Wisconsin
Iowa	Oklahoma	Wyoming

Communications directed to the United States Patent Office in Washington brought no response in the shape of a definition of either the term "Patent Medicine" or the term "Proprietary Medicine."

The State of Connecticut, while not expressly defining the terms "Patent and Proprietary Medicines," does throw some precautions around the selling of what is termed in the law "Proprietary and Patent and Medicinal Compound," but stipulates that such preparations must be put up separately in sealed containers and labeled and accompanied with directions for use, together with the name and address of the manufacturer or distributor.

Maine defines a "Proprietary Medicine" as one which certain individuals, firms, associations or corporations have the exclusive right to manufacture or sell.

New Hampshire defines the term "Proprietary Article" to mean any chemical, drug or similar preparation used in the treatment of diseases, if such article is protected against free competition as to name, product, composition or process of manufacture, by secrecy, patent or copyright, or by any other means.

While New Jersey used the terms "Patent and Proprietary Medicines" in its law, it does not define the terms, but the suggestion is made in a communication from New Jersey that the report of the Commission on Proprietary Medicine of the AMERICAN PHARMACEUTICAL ASSOCIATION be checked up for definitions. Your committee has not consulted this report and is therefore unable to embody in the present report the information that might be derived from that source.

New York reports that this problem has been given attention by the New York State Board of Pharmacy and after considerable thought the determination reached by that board was that a Proprietary Medicine is a medicine that any person or persons have the exclusive right to manufacture or sell.

South Dakota defines the term as follows: "For the purpose of this Act, patent or proprietary medicines shall be considered to include any medicine or drug which is prepared or compounded in proprietary form and sold at retail in the original packages and where the sale thereof is unregulated under the laws of the state."

Virginia attempts to define the terms as follows: "The term patent or proprietary medicines, as used in this chapter, shall include only medicines prepared according to a private formula or a secret process or under a trade-mark of the manufacturer or owner and sold under a trade name in an original package on which appear the disease or diseases for which the medicine is intended to be used and specific directions for its administration."

It will be observed that in the few instances where there has been an attempt made to define the terms as embodied in the laws the definitions are deplorably inadequate to control the situation which exists in most states. It would appear, therefore, that a further study of this subject should be made. In all instances where there has been an effort to define the terms, the definitions have failed to differentiate between that large class of products commonly regarded in the drug trade as classifiable under the term "Patent Medicine" from that other large and ever increasing group known to the drug trade as "Proprietary" products. The result is that in most states merchants

who know nothing of pharmacy are able to stock and sell many dangerous and potent proprietary products, and we believe that the public interest is not sufficiently safeguarded under such an arrangement.

While the definition in the Virginia law is largely inadequate and has been criticized as out of line with the Federal Pure Food and Drugs Act, it does at least have the merit of precluding the sale by general merchants of such proprietary products as do not have designated on their labels the disease or diseases for which the products are intended to be used. Such a provision in state law, while entirely out of line with the thoughts of many of those who are interested in an adequate Federal Act to control the sale of products for self-medication, may be useful until some better solution of the problem is suggested.

It seems to me that the situation would require a clean-cut definition for that group of remedies offered to the public for self-administration, and which we have loosely designated as Patent Medicines; and another clean-cut definition to embrace that group of proprietary products carried in drug stocks ostensibly for the filling of physicians' prescriptions, and commonly referred to as proprietary products. In other words these two groups should be segregated, clearly designated by adequate definitions and the suggestion then made to the several states for a revision of their state pharmacy laws in such a manner as to permit, if desired, the sale of patent medicines by general merchants and to prohibit the sale of proprietary products by that group.

It is common knowledge that the term "Patent Medicine" is a misnomer. Few of these remedies are protected by patents. Some are registered and some are protected by copyright and trade-mark, but these forms of protection are indiscriminately used in the patent medicine field and in the proprietary medicine field.

It is undoubtedly true that many dangerous proprietary products are stocked and sold by general merchants when as a matter of common protection of the consuming public, these products should be distributed only by pharmacists upon physicians' prescriptions. The situation is one which we believe worthy of further study and this inadequate report is presented with the hope that the questions will be placed in the hands of a competent committee for further study and a more definite and constructive recommendation.

Respectfully submitted,

GEO. W. MATHER, New York
JOHN M. WOODSIDE, Pennsylvania
M. N. FORD, Ohio
R. P. FISCHELIS, New Jersey
R. L. SWAIN, Maryland
A. L. I. WINNE, *Chairman*, Virginia.

Subsequent to the making up of the above report, the following letter was received from Secretary Baker of the Colorado Board of Pharmacy:

Mr. A. L. I. Winne, Secretary
Virginia Board of Pharmacy
105 State Office Building
Richmond, Virginia

Denver, Colo.
April 30, 1934.

Dear Mr. Winne:

Replying to your letter of the 18th, I wish to advise that our Board of Pharmacy has defined "Patent" and "Proprietary" medicines, as follows:

"A patent medicine is one the formula of which is registered in the United States Patent Office at Washington, D. C., which registration protects the inventor of the formula from duplication by any other or manufacturing company."

"A proprietary medicine is a medicine compounded according to a formula known only to the manufacturer and marketed under a trade name. This trade name does not necessarily have to be registered under the United States Trade-Mark Laws, as common law trade-marks exist in the United States, and a suit for infringement of a trade-mark may be brought by the original user thereof even though the original user may never have registered the same."

The exemption of proprietary medicines in our Pharmacy Law does not apply to official preparations listed in the United States Pharmacopœia and the National Formulary which are sold under a proprietary name.

Very truly yours,

(Signed) ARTHUR D. BAKER, *Secretary.*

At the conclusion of Mr. Winne's paper a motion was made and adopted, whereby a committee on Patent and Proprietary Medicines was ordered continued, and the report adopted.

Chairman Swain next reported that W. S. Frisbie of the United States Department of Agriculture could not be present and if he submitted a paper on "Coöperation between Federal and State Officials in the Enforcement of the Food and Drugs Acts," such paper will be published.

Chairman Swain next referred to a paper submitted by **William F. Reindollar** of the Bureau of Chemistry, Maryland State Department of Health on "Relationship of the Control Laboratory to Enforcement under the Food and Drugs Act," as follows:

RELATIONSHIP OF THE CONTROL LABORATORY TO ENFORCEMENT UNDER THE FOOD AND DRUGS ACT.

There is perhaps no phase of the enforcement of the Food and Drugs Act more fundamental than that involving the collection, inspection and examination of those products which are offered for sale within the scope of the Act. The very purpose of defining the terms "adulteration" and "misbranding," the very act of creating standards of purity, quality and strength, presuppose the existence of an agency, capable and qualified, to make analyses of the products in question, and to pass critical judgment upon them with respect to these provisions. Hence, the necessity of an adequate control laboratory as an integral cog in the machinery of law enforcement is a well-established and unquestioned fact. The presence of such units in the organizations of the several Municipal and State Health Departments, in addition to those of the Federal Government, is but another confirmation of their value.

The details of the operations of the Control Laboratory and the history of the "official sample" in its course of travel from vendor to analyst form an engaging narrative to those whose interests lie in this field. It is the purpose of this article to outline briefly the procedures adopted to assure the integrity and safeguard the identity of the official sample, and to do this in such a manner that neither jury nor defending attorney may harbor doubts regarding its genuineness or its relation to the vendor.

Purchases of foods and drug products offered for sale on the open market are made in most cases direct from the wholesaler or retailer by an inspector, who is an agent of the Control Commissioner. No effort is made upon the part of this individual either to conceal or reveal his identity, or upon questioning to hide the purpose for which his purchase is being made. However, unless previous circumstances indicate a probable prosecution, or unless the vendor so requests, the samples are not sealed on the premises. The inspector makes notes concerning the places which he visits and when necessary puts an identifying mark on containers; this together with the labels on the package serves to identify the samples for him when he seals them at the end of the day. There is much to be said pro and con regarding this procedure. While in the past it was the custom to seal the sample in the presence of the vendor and although from the legal point of view, this is perhaps the more sound method, because of many disadvantages arising therefrom, it has been discontinued. To begin with it is time consuming, it involves the transportation of extra equipment and what is more important, it frequently creates an unfavorable impression upon the customers of the vendor, who enter and see a government agent engaged in collecting and sealing samples. Harmless though it may be, an unpleasant interpretation is usually placed upon it. Furthermore this procedure does not materially safeguard the identity of the sample, it is rather a challenge to the integrity of the inspector, and a device which is useless in any event if that integrity be lacking.

Inspectors are furnished with locked compartments, accessible only to themselves, wherein they may store their samples, until they are ready to be delivered to the laboratory. After an inspection of their labels by the Commissioner the samples are sealed by pasting a strip label over the stopper or lid of the container. This label bears on it, in ink, the date, name of inspector and

an identification or seal number. To further identify the specimen another sticker bearing this same I. R. No. (Inspector's Record Number) is attached. This I. R. No. corresponds to a numbered sheet in the inspector's record book on which is a complete description of information pertinent to the sample, such as name and address of vendor, time and price of purchase, proprietor of establishment, etc. The inspector then delivers his samples to the analyst who checks them against the records and signs for the number that he has received.

Once in the laboratory the samples are kept under lock and key until an examination can be made, at which time the seal is broken by the analyst. As the nature of the specimens usually varies, analytical precedence is given to those that are most unstable. Hence, a group of volatile spirits would be examined before a group of stable alkaloidal tinctures of the Nux Vomica or Belladonna type. In the case of extremely perishable products, such as spirit of ethyl nitrite, facilities of refrigeration are available and employed.

The great majority of the drug samples collected represent chemicals or galenicals official in the U. S. P. and N. F., simple prescriptions and those many common preparations that are prepared extemporaneously in the pharmacy. In addition to these groups and when circumstances warrant, a few proprietary preparations and cosmetics are samples. Those preparations which are official are examined by the official assay when one is given; if there be none, other standard methods such as those recommended by the Association of Official Agricultural Chemists, or those worked out in the Control Laboratories are employed. Simple chemicals are subjected to the tests for purity and identity recommended for them in the official books.

Extemporaneous preparations and prescriptions form an interesting group because they constitute an index of the accuracy and skill of the compounder and are more reliable in this respect than galenicals which in many cases are purchased from the manufacturer. Capsules of acetphenetidin, quinine or salol, percentage solutions of potassium iodide, permanganate or argyrol, mixtures of sodium bicarbonate with the bromides, and solutions of phenol in oil, are examples of this type which may be purchased with or without a prescription. Investigational work of this nature resulted in some rather depressing discoveries at first, but more lately has been compensated for by marked improvement in the majority of cases. In an early group of ten samples of Saturated Solution of Potassium Iodide, which should contain between 97 Gm. and 103 Gm. potassium iodide per 100 cc., the values were found to range from 45 Gm.–88 Gm.; now it is rarely that an illegal sample of this type is met with. Mixtures, as a rule, have been found to be more carefully compounded when ordered on a prescription than when the same combination is requested orally. There are occasional exceptions, however. Recently, a prescription calling for one dram of phenol in four ounces of olive oil was purchased and upon examination was found to contain liquefied phenol and cottonseed oil. In this case both of the ingredients had been substituted.

The Food and Drug Law of Maryland does not include the Shirley Amendment, neither does it provide for the control of cosmetics, hence not many patent medicines nor beautifiers are collected. However, the few that have been examined emphasize the need of such legislation. Bay Rum containing a substantial percentage of methanol has been encountered on the market. Two types of medical crystals sold at exorbitant prices have been shown to consist essentially of sodium sulphate or Glauber's Salt. A large quantity of mercury was present in a bleach cream which was purchased because a woman had been severely burned by using it. A compound purporting to be of value in the treatment of obesity was found to be essentially dextrose. Turpentine made up eighty per cent of the volume of a pneumonia cure. This sample was purchased by a housewife from an unknown peddler who appeared at her door one day, informed her he was a physician and assured her that his medicine "has cured the most severe cases of pneumonia." Although the lady did not have pneumonia, she applied the medicine and acquired second degree burns over a considerable portion of her thorax. The physician did not return.

Medicines for colds, coughs, lung fever, tuberculosis and all pulmonary complaints, canker, scurvy, all diseases arising from uric acid, gastritis, constipation, cramps of the motor nerves, liver, kidney and bladder troubles, pains in the breast and over the heart, all blood diseases, neuralgia, neuritis of the spleen, and swollen joints have from time to time been received. While in most cases they cure, in some the label modestly limits itself to the words "will relieve." And yet, unless the labels contain misstatements regarding the composition of the contents, little progress can be made in the prosecution of their vendors. Therapeutic claims are beyond the pale of food and drug legislation in Maryland.

Upon completion of the analysis duplicate records are prepared, one of which remains in the permanent files of the Bureau of Chemistry, the other is forwarded to the Commissioner. If the sample is legal it is "passed," that is, the records are filed and the sample destroyed. The office of the Commissioner contains in addition to a "daily purchase file," a complete record of products obtained from any one vendor. By this means the "sample history" of any establishment may be obtained immediately. If, however, the sample fails to meet the standards of purity, quality and strength, laid down for it, the seller is notified of the fact and summoned to appear and is thus "afforded an opportunity to present evidence either oral or written, in person or by attorney, showing any fault or error in the findings of the analyst or examiner, or establishing a guaranty from a party residing in this state" from whom he purchased the goods. The analyst is frequently requested to attend these hearings in order to answer technical questions pertaining to the analysis.

Should the case under consideration represent a wilful or flagrant violation of the law, the Commissioner may present the evidence to the Board of Health and request a prosecution of the offending party. Upon the sanction of that body a complete transcript of the case is forwarded to the State's Attorney and a criminal prosecution is initiated. Here begins one of the most important phases of the chemist's work. It is his duty to appear in court, to testify for the control agency and, if necessary, to defend his analyst against opposing experts. The necessity of the appearance of the chemist in person was emphasized recently in a case held in Western Maryland. This case involved the selling of a poison, mercuric chloride, without observing the regulations pertaining to the registration of such products. The chemist did not appear at this case; he sent the analytical sheet instead. The defendant's lawyer admitted the sale but demurred at the introduction of the analytical sheet. The judge sustained the objections, holding that in spite of the official nature of the document the analyst should have been present in person to present his testimony. The barring of this evidence left the state unable to identify the substance as mercuric chloride and the case was lost.

Thus it may be seen that the rôle of the Control Laboratory and its staff in the enforcement of the Food and Drugs Act is both fundamental and necessary. However, this work is not limited to the important functions described above. The staff of the Chemical Bureau engages in numerous researches which have for their purposes the development of new and better assay methods. Studies on preservation have been made to ascertain the optimum condition under which certain galenicals may be kept. An extensive investigation of this nature is being carried out at the present time with hydrogen peroxide. Samples are kept under varying conditions of temperature and sunlight and in different types of containers and their rate of deterioration is recorded. Another activity has been a statistical study of the weights of content of capsules and of powders with the hopes of establishing tolerances for preparations of this type.

In short, the efforts of the Control Laboratory are directed along two channels: (*a*) It aids by chemical analysis and court testimony in the enforcement of the law, (*b*) it endeavors by research to produce information, the utilization of which may make it easier for the manufacturer to produce legitimate products.

At this time A. L. I.Winne, chairman of the Committee on Nominations, made the following report: For *Chairman*, R. L. Swain of Maryland; for *Secretary-Treasurer*, M. N. Ford of Ohio; *Delegate to the House of Delegates*, Joseph P. Murray of Colorado.

Upon motion of Mr. Elkins, seconded by Mr. King, the report of the Committee on Nominations was accepted.

Chairman Schaefer of the Finance Committee made a further report at this time and reported that his Committee had decided to continue their request to individual board members in case the board had not contributed before and ask for any amount that they could contribute. Upon motion of Mr. King, seconded by Mr. Jones, the Committee was ordered continued.

Chairman Swain next reported the different opinions rendered by Attorney-Generals in regard to pharmaceutical law enforcement and it was the request of the Conference that copies of these opinions be mimeographed and furnished to the members.

Chairman Swain advised the Conference that it was his idea to secure from all state boards, blanks and enforcement records in order that they may be used in helping other states that may inquire for such assistance.

Upon motion duly seconded, the Conference then adjourned.

R. L. SWAIN, *Chairman.* M. N. FORD, *Secretary-Treasurer.*

JOINT SESSION OF THE SECTION ON EDUCATION AND LEGISLATION, A. PH. A., CONFERENCE OF PHARMACEUTICAL LAW ENFORCEMENT OFFICIALS AND CONFERENCE OF PHARMACEUTICAL ASSOCIATION SECRETARIES

ABSTRACT OF THE MINUTES HELD IN WASHINGTON, D. C., MAY 10, 1934.

The meeting of the Section on Education and Legislation, A. PH. A., Conference of Pharmaceutical Law Enforcement Officials, and Conference of Pharmaceutical Association Secretaries, convened May 10th, at 8:00 P.M. The meeting was called to order by Chairman George C. Schicks.

The chairman stated that no regular program had been prepared, so it will be in order to bring up matters relating to work being done and contemplated in the different states.

A. L. I. Winne was of the opinion that this was an opportune time to bring up matters along the line suggested for discussion.

J. Lester Hayman said the West Virginia Legislature had been in session for nearly a year. He referred to the sale of medicinal liquors in West Virginia, that now these could only be obtained on a physician's prescription.

As far as he was informed West Virginia is the only state having a law which demands that the sales tax be passed on to the consumer. Sales under five cents are exempted; up to fifty cents, a one cent tax obtains, and to one dollar, 2 cents. The law went into effect April 1st, and indications are that the tax amounts to from $2^1/_2$ to 4 per cent on the gross sales.

Questions were asked relative to the collection of the tax. Mr. Hayman replied, that the tax is considered a 2 per cent tax, that in making sales the money for the tax is dropped in a box for the purpose; a monthly report must be made.

Mr. Winne inquired whether there was evasion and whether many merchants did not base their reports on a 2 per cent tax.

Such possibilities were admitted by Mr. Hayman.

Various other means of evasion were brought out by Messrs. Adams, Winne and Costello and the question was asked whether a person could make a small purchase and later, make another and have the lower sales tax apply to the combined sales. Mr. Hayman replied that this would not be legal. He said that customers at first objected to the tax, but now, seemingly, they do not.

J. M. Plaxco said that South Carolina had a General Sales Tax which was amended to tax certain items by affixing a stamp tax—this applies among other things to soda, cigars, etc.

W. H. Rivard reported on legislation in Rhode Island especially relating to the registration of assistant pharmacists. The law now requires four years of collegiate work and graduation. Provisions were made for assistants to take the Board examination until July 1936. An effort was then made to register all assistants. This was defeated and Rhode Island's law requires four-year prerequisite. This law was fought during the next session and the opposition appealed to the Governor. As chairman, Mr. Rivard and his committee secured petitions to the Governor and also the backing of the medical profession was obtained, the Board of Health was contacted and within three days it was possible to get the Governor's approval. The efforts to defeat the law are being continued and require alertness of pharmacists.

The speaker referred to the Rhode Island law permitting druggists on payment of $100.00 to sell liquors. The ASSOCIATION is strongly opposing the measure.

P. R. Loveland referred to experiences in counteracting sales tax legislation and, especially, the coöperative efforts. The number of retailers representing every branch of business was so large that instead of the meeting being held in the Assembly Chamber it was necessary to adjourn to an auditorium. As a result, the passage of a sales tax has been held up.

C. Leonard O'Connell stated that an effort was made to tax prescriptions under a Pennsylvania mercantile act; this has been amended excluding pharmaceuticals and prescriptions from the tax.

He stated that Pennsylvania pharmacists did not desire to engage in liquor business. Pennsylvania is in the liquor business, has its own stores and leases.

George C. Schicks said that in New Jersey pharmacists must pay a high license to fill liquor prescriptions.

J. B. Pilchard said that in Pennsylvania pharmacists can fill liquor prescriptions without paying a license tax.

R. C. Reese stated that in Kansas they had difficulties with drug stores having no registered pharmacist in charge, especially with stores that have changed hands. Since January this has been corrected to a certain extent.

The Kansas registration act was discussed by Messrs. Reese and Swain.

Secretary Swain inquired relative to State registration acts which give the power of granting or refusing store registration.

B. V. McCullough stated that Indiana required endorsements as to character.

A. L. I. Winne said Virginia granted permits for one year. He regarded the Virginia registration provision as one of the most useful, because there are no inspectors in the State. The permits do not carry the Board Members' signatures, they are signed by the secretary. The application is passed on by the Attorney-General's office, if deemed necessary; the information desired is, the name of the applicant, that of the pharmacist in charge, his hours of duty and the name of the one who is left in charge during the absence of the pharmacist and the hours during which the place of business is open. All the information is sworn to and the owner signifies that he will observe the pharmacy law.

In West Virginia, practically, the same form is in use.

R. L. Swain asked whether the permit registers the pharmacist. Mr. Winne replied that if the owner is not a registered pharmacist, the permit is given in the name of the pharmacist and when he ceases to be employed, the permit is canceled.

Mr. Reese inquired relative to refusal of permit, Mr. Winne replied that if the pharmacy is not notarized, the applicant is notified; in his opinion the safest way is, if the application is in due form, that the permit be issued and take it away if there is non-compliance with the law.

J. J. Gill inquired of C. T. Gilbert regarding the certificate of fitness in Connecticut. He replied that this certificate applied to those making application for State Liquor Control License.

In reply to a question as to the kind of whisky that must be dispensed, R. L. Swain stated that it depends on where the liquor is dispensed. In the District of Columbia, it must be official whisky. The interpretations recently issued by the Food and Drug Administration—when a physician writes a prescription for whisky, the official article must be dispensed, but if the physician states *not* U. S. P., then other whisky can be dispensed. The Government has issued interpretations which will guide the pharmacist in labeling and dispensing. Answering Mr. Brown (Kansas) he referred to an occurrence where a prescription was brought to a pharmacist; being asked the price the customer advised that he could buy the whisky at another store for much less. The pharmacist explained that the whisky he would give the customer was official, but the purchase was made at the other store. He did not argue relative to the quality of the whisky, but it was the duty of the pharmacist, under the law, to dispense official whisky on a prescription.

Mr. Brown inquired if an inspector demanded a pint of whisky and that of the U. S. P. is not in stock, can other liquor be dispensed?

R. L. Swain stated that this opened up a question which was the subject of the celebrated controversy between Dr. Harvey W. Wiley and Mr. Howard Taft. The Pharmacopœia defines Medicinal Whisky. When whisky is called for, he considered it was always a safe procedure to ask whether a straight or blended whisky is desired.

Mr. Swain referred to a session of the Maryland Legislature limited to emergency matters and the most important was enactment of a satisfactory liquor control act for the State of Maryland. Under it alcohol—used for medicinal, antiseptic and toilet preparations, flavoring extracts, and other preparations unfit for beverage purposes—was exempted from the State Excise Tax. Also, pharmacists are permitted to fill prescriptions for intoxicating liquors as defined in the Act without the payment of a State license.

The speaker continued by referring to legislation in Western and Pacific Northwest states relative to house peddling.

A. O. Mickelsen said he had a paper prepared by F. C. Felter. Parts of the paper follow:

CAN HOUSE-TO-HOUSE SELLING BE STOPPED?

BY F. C. FELTER.

The writer welcomes the opportunity to present such information as has developed and is available at this time, concerning the control, through local ordinances, of the evil of house-to-house selling.

It is a fact beyond dispute and well known to your members, that retail druggists and merchants lose thousands upon thousands of dollars in business annually to the house-to-house canvasser. Among the items vended are many which should be sold by the retail druggist; they are deprived of business which should go to them as rent and tax payers and employers of labor in the community. The same is true, of course, of other lines of trade.

Many attempts have been made by municipalities to control this evil practice, most of them being through the license system. In other words, house-to-house canvassing is permitted upon the payment of certain license fees. While this has been partially effective the fact remains that in most localities house-to-house selling and soliciting continues more or less unabated. Some of the larger firms who practice this system of selling pay the licenses and then proceed to take business from the retail merchants. The city treasury is benefited while the retail merchants are deprived of business which they should have. In many other cases the itinerant house-to-house canvasser slips into town, does his canvassing quickly and is gone again. He evades the payment of a license and he takes away revenue which should have remained in the city and been spent with its local merchants.

It has remained for the towns of Rock Springs and Green River, Wyoming, to solve the problem; at least this appears to be the case at the present time. An attorney in Rock Springs is the author of the legislation which has been adopted in both these and other Wyoming cities and which seems to have every promise of withstanding all court attacks as to its constitutionality.

The Green River ordinance was first brought to the attention of the *Pacific Drug Review* late in 1933. The writer, recognizing the new point of approach to the problem, as represented by this ordinance, addressed a letter to the mayor of that city. The letter was turned over to the attorney who had originated the ordinance, Mr. Thomas Seddon Taliaferro, Jr., who promptly wrote, giving not only a copy of the ordinance but details of the court tests by which the ordinance has been thus far upheld as constitutional.

For the purposes of this article it is referred to hereafter as the Green River ordinance. It follows:

"*Be It Ordained* by the Town Council of the Town of Green River, Wyoming:

"Section 1. The practice of going in and upon private residences in the town of Green River, Wyoming, by solicitors, peddlers, hawkers, itinerant merchants and transient vendors of merchandise not having been requested or invited so to do by the owner or owners, occupant or occupants of said private residence, for the purpose of soliciting orders for the sale of goods, wares and merchandise, and/or for the purpose of disposing of and/or peddling or hawking the same, is hereby declared to be a nuisance, and punishable as such nuisance as a misdemeanor.

"Section 2. The town marshall and police force of the town of Green River are hereby required and directed to suppress the same, and to abate any such nuisance as is described in the first section of this ordinance.

"Section 3. Any person convicted of perpetrating a nuisance as described and prohibited in the first section of this ordinance, upon conviction thereof shall be fined a sum of not less than twenty-five (25) dollars, or not more than one hundred (100) dollars, together with costs of proceedings, which said fine may be satisfied, if not paid in cash, by execution against the person of any one convicted of committing the misdemeanor herein prohibited.

"Section 4. All ordinances and parts of ordinances in conflict with this ordinance are hereby repealed.

"Section 5. It being deemed by the town council of the town of Green River that an emergency exists, this ordinance shall be in force and effect from and after its passage and approval.

"(Note: In Rock Springs, Wyo., the ordinance also specifically prohibits solicitors for building and loan, insurance, newspapers, books, pictures and periodicals.)"

The writer determined to try to interest retail druggists throughout the Pacific slope field in the passage of similar ordinances in their cities. It was, and still is, held by the writer that retail druggists in almost every city could, if they would interest themselves in this legislation, secure its passage by interesting retailers in other lines and, through the local Chamber of Commerce or women's organizations or both, secure its adoption.

Your attention is directed to the fact that the Green River ordinance declares "the practice of going in and upon private residences in the town of Green River, Wyoming, by solicitors, peddlers, hawkers, itinerant merchants and transient vendors of merchandise, *not having been requested or invited* so to do by the owner or owners, occupant or occupants of said private residence, for the purpose of soliciting orders for the sale of goods, wares and merchandise, and/or for the purpose of disposing of and/or peddling or hawking the same, is hereby declared to be a nuisance."

And a nuisance it is. Housewives will tell you so.

Not only is the practice of ringing doorbells at all hours of the day a nuisance to the housewife but the entrance of itinerant vendors, hawkers, peddlers, etc., upon private property often leads to some sort of crime. The solicitor, vendor or peddler may, through artifice or otherwise, gain entrance to the residence for the purpose of securing certain information which would later lead to robbery. He may, through his persuasiveness or force of salesmanship, dupe the housewife into trading off valuable securities for worthless stocks or merchandise. He frequently sells the housewife something that she does not need or want or secures a contract for some long payment scheme which becomes a burden upon the head of the house. He always takes revenue from that particular town or city which should be spent with its local merchants.

Declaration of the "uninvited" entrance upon private property by these vendors as "a nuisance" is wholly within the police powers of any municipality. This has been affirmed by the United States Circuit Court of Appeals, Tenth Circuit, where the Green River ordinance was upheld as constitutional. The Fuller Brush Company attacked the Green River ordinance and won its case in the District Court. The town of Green River appealed the case to the United States Circuit Court of Appeals. The case was decided May 11, 1933, and is reported in the 65th Federal, 2nd Edition, page 112. The Appeals Court reversed the District Court and sustained the ordinance as being constitutional and within the police power of said town.

Among other things the court also said: "The frequent ringing of doorbells or private residences by itinerant vendors and solicitors is, in fact, a nuisance to the occupants," and quoted from a decision of the United States Supreme Court as follows:

> "This court has frequently affirmed that the local authorities intrusted with the regulation of such matters, and not the courts, are primarily the judges of the necessities of local situations calling for such legislation; and the courts may only interfere with laws or ordinances passed in pursuance of the police power where they are so arbitrary as to be palpably and unmistakably in excess of any reasonable exercise of the authority conferred."

The writer is informed by Mr. Taliaferro that the time limit for appealing this case to the United States Supreme Court has long passed.

It would appear, therefore, that the Green River ordinance, declaring certain practices as a nuisance, is constitutional and will stand in the courts of most states. The Corporation Counsel of Seattle, Washington, declares this as his belief. A prominent firm of attorneys in Portland, to whom the writer submitted the ordinance, said: "It is our opinion that to abate a nuisance is strictly within the police powers of any legislative body, whether state or city."

A law student, writing in the *Rocky Mountain Law Review* of the University of Colorado, who had made a particular study of this ordinance, said: "This Green River case may well be in later years looked upon as a landmark in this type of legislation."

So much for the facts as to the law itself and the courts' decisions and legal opinions.

Now, just a word in conclusion. As a result of the writer's efforts a number of cities in the Pacific slope field have started movements to have this legislation enacted. Santa Rosa, Cali-

fornia, Prineville, Oregon, Yoncalla, Oregon and Lovell, Wyo., have already adopted the ordinance through the efforts of the retail druggists of those cities. Probably fifty other cities of varying sizes in the Pacific slope field have initiated movements to have it placed on the statute books.

It is the writer's belief that if the retail druggists in any town or city will band themselves together and work with the other retailers, this legislation can be passed. It should be a simple matter to get women's organizations behind it as well as the local Chamber of Commerce, and the pressure of these bodies upon the city fathers would secure the desired results.

J. J. Gill stated that an effort had been made in Providence to pass such an ordinance, but unsuccessfully.

On motion duly seconded it was voted to accept the paper for publication.

R. L. Swain spoke of methods employed by the vendors. He stated that the prices charged by these vendors were considerably higher than those of the average drug store. Some of the vendors make the statement that they represent an organization and in that way secure a hearing.

A. O. Mickelsen referred to the City Ordinance of Savannah, Ga., which had not been tested in courts, but, in part, has been considered unconstitutional. Mr. Elkins, of Georgia, stated that the city attorney of Savannah held that the ordinance was in conflict with the state law. The Georgia law permits the sale of patent and home remedies by General Merchants. The Attorney-General ruled that the names of the home remedies would have to be enumerated. The Georgia law defines patent and proprietary as meaning the same. General Merchants cannot sell pharmaceuticals.

R. L. Swain inquired of Mr. Elkins whether the Attorney-General had ruled that the law enforcement officer shall construe the general terms.

Mr. Elkins replied that the Attorney-General held there was no one else to enumerate them. Mr. Swain discussed various opinions relative to the terms "patent medicines, home remedies," etc. He suggested that when questions came up regarding court decisions, that members address Secretary M. N. Ford. He referred to the opinion of the Attorney-General (Hon. Carey D. Landis) of Florida, which states that the Pharmacy Act (13757, 1929) restricts in every sense of the word the sale of all medicinals to registered pharmacists.

James H. Beal said he had been asked for his opinion of that of the Attorney-General. His reply was that if it can be sustained Florida has the best pharmacy law in the United States and as long as the Attorney-General is willing to defend it, let it stand.

He also approved of the enforcement by the State Board of Health. The defendant's Attorney cannot say the druggists are trying to monopolize—the State Board of Health enforces that part of the act. Some have been desirous to strike out the provision which assesses registered pharmacists ten dollars annually for the support of the State Board of Health. He advised that it was the cheapest law enforcement they could have. Dr. Beal referred to several stores which were compelled to take down the signs advertising "family medicines" and "domestic medicines." He was inclined to believe the supreme court would uphold the Attorney-General.

F. W. Meissner inquired relative to the meaning of a store being "in immediate charge of a registered pharmacist." Dr. Beal replied that if an inspector took up a specimen and no registered pharmacist was in charge, it would be construed as no registered pharmacist in charge.

Mr. Elkins referred to the Savannah ordinance having been introduced by the Board of Health as helpful.

Dr. Beal said restriction of the sales of medicine was for public safety, public welfare. His recollection is that physicians, under the Florida law, are given reasonable liberty in handling chemicals, biologicals, etc.

R. L. Swain stated that about 1918 Dr. E. F. Kelly conceived the idea expressed by Dr. Beal, that perhaps pharmacists were wrong; they were rendering a Public Health service and should not pay for the enforcement of the Act any more than a grocer should pay for police protection. The first step was to place a pharmacist on the State Board of Health of Maryland. In 1922 the Food and Drugs Act was so amended.

Dr. Swain said, they asked the Governor if he would finance the enforcement of the Pharmacy laws and he replied that he could not, as he had made a pledge to simplify state government, but if a place could be found in the existing state government where the activities would fit in he would finance them, and so the Food and Drugs Act was amended. Instead of the pharmacists of

the state of Maryland paying $10.00 per year the Governor sees to it that $15,000.00 is made available for enforcing the pharmacy acts.

The speaker stated that if the enforcement program of the state and the legislative program can be tied up with the general health program a great deal of criticism is disarmed. Instead of being purely a Board of Pharmacy program it is a part of the health program of the state; the same as vaccination laws and the like.

Dr. Swain presented two Attorney-General's opinions, one of them deals with Mr. Meissner's question, namely, when is a registered pharmacist in charge? The Maryland Act demands that a registered pharmacist must be in charge of a store.

He said further, that in Maryland they had some difficulty with the supervision of the registration of poison sales. He once heard Dr. Beal make the statement that an enlightened pharmacist would be diligent in his observations of the poison laws; this he referred to, chiefly, because no other dealer is going to do that. He is not going to the trouble that a pharmacist will in handling poisons. He presented a number of experiences. Several applied to various phases of the subject presented by Dr. Swain.

C. T. Gilbert spoke on the limitations of opening new stores in Connecticut, especially the conversion of perfume shops into drug stores. A recent law requires registration of a new store and for this $200.00 is charged. Only about five stores have been registered since its passage, before that the number was from twenty to seventy-five each year.

R. C. Wilson stated that in Georgia they were considering compulsory registration laws and he asked Walter D. Adams to explain the Texas law. Mr. Adams stated that this had been presented last year and published in the JOURNAL. The question, however, relative to the constitutionality of Section 14 of the Pharmacy Law; this had been declared unconstitutional by the Attorney-General. The ASSOCIATION has brought a friendly suit against the Board of Pharmacy for the money which the Board has collected. It is assumed that the money does not belong to the state and if it does not go to the ASSOCIATION then it will remain with the Board of Pharmacy. It is proposed to take the case to the Supreme Court, if necessary. Mr. Adams also advised that the bill providing for a sales tax was defeated in Texas.

R. P. Fischelis referred to three bills that had been introduced in the New Jersey Legislature, one of them provides for the revocation of licenses of registered pharmacists for crimes involving the violation of the narcotic and liquor law and for non-compliance with the Pharmacy Act. The case came up a year or more ago when a pharmacist who had served time for violation because of the sale of wood alcohol for beverage purposes had served that term and applied to the Board for reinstatement, that is, renewal of his registration. The Board felt that he was not a proper person to be registered and the question was brought to the attention of the Attorney-General who found that the Pharmacy Law did not provide for revocation of licenses for crimes involving moral turpitude. Three years after the first occurrence this same pharmacist was convicted of forging narcotic prescriptions and again committed to jail and the Judge rather severely criticized the Board of Pharmacy for permitting that type of individual to continue the practice of pharmacy. Then it was pointed out to the Judge that the Attorney-General had ruled that the law did not provide for revocation in such cases. A strong letter was sent to the Legislature, but up to this time has not been passed.

A second bill was introduced which passed both houses and was signed by the Governor, providing for the annual registration of the pharmacies. Whenever this bill came up it included a definition for the terms "drug store" and "pharmacy" and found objectors and so it was decided not to define the terms "pharmacy" and "drug store." That was made possible by the fact that an Act was passed in 1932 limiting the use of terms "pharmacy" and "drug store" and "apothecary shop" to establishments operated under the supervision of a pharmacist.

The third piece legislation provided for a grant of power to the Board of Pharmacy to appeal to the Court of Chancery for injunctions to prevent the continuous violation of the law. The Board is more interested in law enforcement and the proper conduct of pharmacists than in collecting penalties. This legislation has not been passed. There was also introduced, without any intervention from pharmacists, a general resolution asking for investigation of cut-rate cosmetics shops and chain drug stores. The joint resolution provided for the establishment of a commission consisting of two members of the Senate, two members of the Assembly and two members of the State Board of Pharmacy; this has passed the house and is now pending in the Senate.

L. L. Walton inquired whether Dr. Swain had discussed with the Attorney-General the character of the evidence that would be required in order to convict for conducting a pharmacy without having a registered pharmacist in charge. He replied, that in Baltimore there is a working agreement with the State's Attorney for the City and he has requested that cases be brought to the magistrate courts. This prevents cluttering up the State docket, but if there are difficulties then the case comes back to the Attorney-General. The magistrates have invariably said, that if cases are brought before them that there should be real evidence. The decision has only come a few days ago and no effort has been made, so far, to put it into effect, but the Act states, that at no time should a pharmacist be left in charge, who is not registered.

Mr. Walton said that in Pennsylvania the State Board has been operating under the decision, for the last five to seven years, which holds that the pharmacist does not lose charge of the pharmacy by going out to meals or by being absent for one-half day. It has also been held that in order to prosecute there must be a sale.

Dr. Swain quoted from the Act which states no pharmacy shall at any time be left in charge of a person who is not a registered pharmacist. It is based upon the selling of drugs or medicines or compounding and is simply a blanket statement.

Mr. Walton stated that the Pennsylvania law was effective along that line.

Dr. Swain was of the opinion that a short absence from the store would not be sufficient to convict. He referred to a case in Baltimore when a pharmacist left the store and gave explicit instructions that he was going out. He had also left a man in charge with the instruction not to fill any prescriptions or sell poisons during his absence. The case came before Judge Owens and he said that the advice given was all right for the individuals concerned but did not take into consideration the many people of the city of Baltimore.

Dr. Swain explained that in Maryland and Missouri a jury is the judge of both the law and the facts. In most states a court instructs a jury in the interpretation of the law in a criminal case, but in Maryland this is not so. The court may refuse to give instructions or, when requested, to give them. The instructions must be given in this way, "Gentlemen of the Jury, in response to your counsel's request, your counsel requested that I interpret this act to you, but bear in mind, under the constitution of the state of Maryland you are the judge of the law and the facts and you are in no sense obliged to follow it and you may disregard it." So that applies to the case referred to. It depends on the decision reached by the jury.

Mr. Walton stated that in Pennsylvania a great many pharmacies are conducted by one registered pharmacist only and the Board has hesitated to penalize the pharmacist who leaves his store for a brief period.

M. N. Ford referred to a case in Ohio. It was an appeal case. The case came to trial and the defendant stated that he was in full and actual charge as the law provided, that he was in daily charge of the store either by telephone, telegraph or by letter. The case went against him and the Board was sustained by the Court of Appeals.

W. B. Philip stated that the decision from the Attorney-General of Maryland is legally correct, but he would be surprised if a lower court would convict and he spoke from experience, but considered the decision from the Attorney-General a very interesting one. He felt that the decision was a useful one, even if it could not be carried into effect in every instance.

R. P. Fischelis referred to a case in New Jersey where the pharmacist was frequently absent and his wife was left in charge. She would not sell anything that conflicted with the law, but a sign was displayed and this was called to the attention of the Attorney-General; he suggested that photographs be taken at various intervals during which the store was not in charge of the pharmacist. The Board went to court with that evidence and a conviction was given. There were four days in which no pharmacist was in charge of the store. In the case of persistent violations the proceedings should be taken down and the judge of the lower court will give careful consideration before rendering his decision.

A. L. I. Winne stated that he had an experience when the Virginia Assembly met and there were several measures under consideration that affected pharmacists and merchants. They were interested in issuing retail licenses and wholesale licenses and quite a number of different activities were concerned, so he found himself drawn into a formed organization representing about 26 groups. These worked together in the interest of a tax by which the Governor was endeavoring to raise a million dollars for schools. To a certain extent they were successful, but the interesting thing was the possibility of such a line-up for working together for legislation.

J. Lester Hayman stated that they had a bill before the Legislature which was sponsored by hotel and restaurant people. In it was a section which evidently was overlooked; it provided that where medicines were prepared and sold this department must be separated from the rest of the establishment by sound-proof partitions from the ceiling to the floor and this concerned many pharmacists.

M. N. Ford referred to the filling of prescriptions for whisky involving a question before the Supreme Court at this time. A liquor control act was passed a few months ago and in order to take care of the business until an organization was made effective the control was wished upon the Board of Pharmacy. These permits were issued to about one-half of the druggists of the state and the question was raised as to what was whisky. The druggists had to stop selling whisky and take out permits to fill prescriptions only.

Recently an individual tax payer of the state filed suit against the State Liquor Control Board for selling or contemplating to sell blended whisky. This is now before the Supreme Court.

W. Bruce Philip referred to House Bill 3758 changing the designation "Retail Liquor Dealer Tax" to "Medicinal Tax." It is now before the Senate Finance Committee of which Senator King is the chairman. The meeting was then adjourned.

The British Pharmaceutical Codex. Published by direction of the Council of the Pharmaceutical Society of Great Britain. The Pharmaceutical Press, 23 Bloomsbury Square, W. C. 1, London, England. Price 35 shillings, foreign postage extra; the price does not include duty.

Various supplements antedating the Codex have appeared in England since early in the last century, the purpose being to provide recognized formulas for medicines which were not official in the British Empire, Gray's Supplement was first published in 1818 and was subsequently edited by Professor Redwood; other publications followed which met with more or less favor according to standing of the author or compiler, but without recognition beyond that.

The need for a work issued under the authority of some statutory body was expressed by resolution in 1904 and responsive thereto a committee was organized by the British Pharmaceutical Society for carrying the purpose declared in the resolution into effect. The chairman of the committee was Michael Carteighe; the sub-committee in charge of the collection of data and information was made up of members well and favorably known to pharmacy, among them Dr. W. E. Dixon, Prof. H. G. Greenish (deceased). The research work required for the solution of problems was performed partly in the Laboratory of the British Pharmaceutical Society, in the teaching institutions and of individual members of the Society.

The scope of the work was defined by describing it as "an Imperial Dispensatory for the use of medical practitioners and pharmacists," and named—"The British Pharmaceutical Codex."

The general plan has been followed, with revisions and additions, in the contents and arrangement and keeping step with the progress in pharmacy and changes in materia medica.

Two of the more important changes in the revision of the edition of 1907 were the additions of brief descriptive notes on the preparations of each drug and chemical at the end of the respective monographs and the inclusion of a pharmacological and therapeutic index.

Other parts of the book in its several editions have been prompted by revisions of pharmacopœias and official formularies and developments in materia medica and therapeutics, and improvements and suggestions which have given greater value to the Codex.

About one thousand substances have been given consideration in monographs; in addition, matters relating to chemical and physical properties or botanical characters, action and uses and summary of preparations, new remedies, sources of proprietary preparations, information relative to vaccines, vitamins, etc. In general, it may be said that the plan of the Codex does not differ greatly from American dispensatories. A comprehensive index is included and the subjects are considered in four general divisions: Part I, General Monographs on Chemicals, Crude Drugs, etc. Part II, Surgical Dressings. Part III, Formulary. Part IV, Appendices—tables, general tests, reagents, methods of sterilization, pharmacological index, trade names, proprietary substances, etc.

EDITORIAL NOTES

PHARMACISTS ALWAYS DO THEIR PART.

The Christmas Seal this year commemorates the 50th anniversary of the beginning of modern sanatorium treatment in the United States by the late Dr. Edward Livingston Trudeau at Saranac Lake, New York, in February 1885. The one room cottage the seal depicts became the nucleus of the sanatorium movement in this country. To-day there are 659 sanatoria containing a total of 86,917 beds. The cottage, called the "Little Red" because of its color, is preserved at the institution founded by Dr. Trudeau.

JOHN WESLEY'S KNOWLEDGE OF MEDICINE.

Repetition of the following article may be of interest to some of the members of the AMERICAN PHARMACEUTICAL ASSOCIATION at this time, because of the anniversary celebration of the founding of the Methodist Church. Reference is also made to an article in the May number of the JOURNAL for 1929, page 523. Through the kindness of Lawrence Williams, of Baltimore the ASSOCIATION is in possession of a copy of "Wesley's Formulary," 26th edition.

A. Mortimer, writing in the "Special Issue" of the *Chemist and Druggist*, June 25, 1921, states that in all references to John Wesley and his life-work, he has read, the knowledge of medicine possessed by Wesley seems to have been ignored. Mr. Mortimer presents a number of abstracts from "Primitive Physic: or an easy and natural method of curing most diseases," by John Wesley. These books were advertised to be sold *at the Rev. Mr. Wesley's Preaching-Houses in Town and Country*. The preface to the first edition is dated June 11, 1747; a bibliographer has ascertained that the book treats of 243 ailments and contains 725 recipes. The history of medicine is briefly traced in the preface and the following is taken from the article referred to: "In the early days physic," says Wesley, "as well as religion was chiefly traditional. Father handed down to son what he himself had in like manner received, concerning the manner of healing both outward hurts and the diseases incident to each climate, and the medicines which were of the greatest efficiency for the cure of each disorder. Then, when it was seen how the beasts would use certain natural remedies to cure their ills, they were tried for human beings with good results, and experience and physic grew up together. In addition to this knowledge, many accidental discoveries were made which led to the wider use of many hitherto unknown remedies. Hence rules for the application of these, and medical books were immensely multiplied, till at length physic became an abstruse science, quite out of the reach of ordinary men. Physicians, men who knew a little more about medicine than the average person, now were held in esteem, as persons who were something more than human. Profit attended their employ as well as honour; so they had now two weighty reasons for keeping the bulk of mankind at a distance, that they might not pry into the mysteries of the profession." Wesley then goes on to show that the medical men of the time of which he is speaking insisted that a knowledge of anatomy, natural philosophy, and even astronomy and astrology were necessary to the understanding of the art of healing. They introduced complex medicines consisting of so many ingredients that it was impossible to know which wrought the cure.

U. S. RADIUM IMPORTS.

The Belgium Congo has been the world's chief source of radium, although some has been produced in Czechoslovakia and, in 1930, radium ore was discovered in northern Canada.

According to C. C. Concannon, chief of the Commerce Department's Chemical Division, radium is by far the most valuable commodity ever produced. While the United States is the world's largest consumer it has imported less than one-third of one pound of the substance during the last decade and for this small amount has paid more than $6,000,000.00. During this period imports have remained fairly steady at around 125 to 170 grains valued at from $400,000.00 to $575,000.00 per

annum, until 1930 when imports advanced to 260 grains valued at $925,000.00, the largest amount ever imported during one year. In 1933, 179 grains valued at $576,000.00 were imported, at an average invoice price of $3217.00 per grain, and during the first seven months of the current year $400,000.00 worth was purchased abroad, it was stated.

The bulk of radium imports comes from Belgium which controls the Congo output, while smaller consignments are received from Canada and elsewhere.

TETANUS TREATED WITH CURARE.

Curare has recently had its value assessed in the treatment of tetanus. Two cases are reported; in the first, a laborer (39), four doses of "gourd" curare, each 0.032 Gm. was given subcutaneously at six-hourly intervals on the eleventh day following the injury and four days after the onset of tetanus symptoms. Within two hours of beginning the treatment the spasms were less severe, the patient had less pain and was more comfortable. The improvement continued for forty-eight hours, later, by another injection, 0.032 Gm. was given. The patient ultimately recovered. In the second case, a boy aged 7, an initial dose of 0.0075 Gm. was given subcutaneously, followed in ten minutes by the same amount, after a further ten minutes by 0.015 Gm. and forty minutes after the first dose with another one of 0.015 Gm. By this time the rigidity had disappeared, but respiratory difficulty followed and the patient died. Both patients received, in addition, routine treatment with tetanus antitoxin.—(*Lancet* (1934), 5792, 475.)

NEW YORK BOTANICAL GARDEN CATALOGS ITS PLANT NAMES.

An important research project, which has already begun to prove its value, has been completed at the New York Botanical Garden through the assignment of unemployed persons by the Works Division of the Department of Public Welfare. This is the compilation of the Index Kewensis, a series of six loose-leaf volumes containing the generic and specific names of plants and all the sources of technical knowledge available. It represents one of the romances of scientific research, and is said to be the only one of its kind.

OVERDOSE OF PARALDEHYDE.

Evidence was given by a nurse of the hospital (Fettercairn Hospital, Hamilton, Australia) that she had telephoned to a chemist for eight drachms of paraldehyde. This paraldehyde had been injected as a preanesthetic.

The apprentice of the chemist in evidence said he had taken the telephone message, which was an order for eight ounces of paraldehyde. The coroner found that death was caused by heart failure, due to paraldehyde poison, and accelerated by extensive pleural adhesions to both lungs, and a flat and flabby heart. He found that the quantity of paraldehyde administered was eight ounces, whereas the quantity prescribed was eight drachms, and that the excessive quantity given was due to a mistake made in the preparation and administration of the drug by a qualified, certificated nurse. He also found that when unfavorable symptoms manifested themselves every effort was made to restore animation.

FOR REAL PHARMACAL SERVICE.

"Every branch of the drug trade must recognize the importance, with respect to the general welfare, of the pharmacist in the retail drug store. If it were not for the confidence justly placed by the public in the local pharmacist, many of the opportunities and privileges of the drug trade would not exist. It cannot be questioned that as public confidence in the pharmacist may lessen, as the drug store may become less and less an institution of public health, the rights of manufacturers of drugs and medicinal preparations will be restricted by legislation enacted in the public interest.

"Certain consumer interests, largely miscalled and almost wholly self-appointed, have not been idle in recent months in the matter of stripping the drug industry of important privileges. One of the objectives is the supplanting of the existing pharmacally prepared official standards for drugs with government-made standards. It is, of course, the professional pharmacist who represents the professional work of the drug industry in the eyes of the public. It is imperative, therefore, that he should be truly representative of the highest ideals and purposes of his calling. It is equally necessary that these ideals and purposes be maintained on the highest possible plane."—From an editorial—*Oil, Paint and Drug Reporter*—September 3, 1934.

PERSONAL AND NEWS ITEMS.

Fred B. Kilmer has been active in compiling historical data and exhibits of Christ Church,

New Brunswick, organized in 1742. Even brief records are impossible; however the exhibit of a photostatic copy of a deed or lease from Philip French Esq. is referred to as a long time lease. The document is a lease for 2000 years from December 4, 1742, for the plot of ground 150 x 150 feet on which the church now stands; the lease will expire in 3742 and the annual rental named is "two peppercorns per year, if demanded."

Among recent visitors at the American Institute of Pharmacy were: Dr. Walter Schmid, Dresden, Germany; Dr. Julius F. Leo, Dresden; the former is food and pharmaceutical chemist and the latter's pharmacy recently celebrated its 450th anniversary. Among other visitors—Miss Grace I. Harper, registrar of Rutgers University College of Pharmacy; Fred A. Lawson, Stoneham, Mass.; Mrs. C. H. Huntley, New Haven, Conn.; Charles G. Ajax (and wife) president of Washington State Pharmaceutical Association; Floyd B. Johnson, Calhoun, Ga.

The interest of the Press, in the American Institute of Pharmacy is shown by publishing brief sketches and pictures of the building. We have before us a clipping with an excellent print of the *Kerkhoven*, Minn., *Banner*, under date of September 7th.

Dr. Walter and Dr. Ida Noddack, Berlin, have been awarded the Scheele Medal of the Swedish Chemical Society.

Prof. Georg Gamow, head of the department of physics and mathematics at the Polytechnic Institute at Leningrad, has been appointed visiting professor at the George Washington University for the coming year. During the summer Dr. Gamow was a foreign visiting member at the twelfth annual physics symposium of the summer session of the University of Michigan. At George Washington University he will give a seminar in theoretical physics and will continue his research on the atomic nucleus.

E. W. Runyon, member of the A. PH. A., since 1875, has returned from England after a two months' sojourn and is again at his desk.

Edgar Warfield, Alexandria, Va., veteran pharmacist (aged 92 years), after 78 years of service is still active in his profession. In a picture of the *Evening Star*, Washington, September 6th, he is shown with his son and grandson in the prescription department. This is no unusual occurrence, for he comes to the store every day.

A. B. Stevens, member of the A. PH. A., since 1885, former dean of the College of Pharmacy, University of Michigan, now of Escondido, Calif., has been spending several weeks in Ann Arbor. A dinner party was given for him by **Prof. and Mrs. C. C. Glover,** members of the family and former associates were present.

Prof. Justin L. Powers is pursuing graduate work in the University of Wisconsin.

Secretary H. C. Christensen, chairman of the Pharmacy Exhibit at the World's Fair, and Mrs. Christensen celebrated their forty-first wedding anniversary at the Swiss Village, A Century of Progress, September 6th. Mr. and Mrs. A. Finstead, of Miami, Fla., were honored guests of the occasion.

Prof. G. Barger was presented with the Hanbury Medal at the opening of the 93rd session of the School of Pharmacy,[1] of the British Pharmaceutical Society, on October 3rd. Professor Barger is not a pharmacist; he is Professor of Chemistry in relation to medicine in the University of Edinburgh, and is well known for his work on ergot and jointly with Dr. F. H. Carr was a discoverer of ergotoxine.

Director Claudius T. Murchison, of the Bureau of Foreign and Domestic Commerce, delivered a radio address to the National Industrial Advertisers' Association, during their meeting in Cincinnati. On September 21st, Mr. Murchison gave a historical résumé of the development of machinery in the industrial world. This has created problems and produced triumphs. The achievements of the machine should be preserved and fostered not only in the interest of society, but in the interest of profitable business. The problem is, what can be done to improve conditions?

A. R. L. Dohme has presented to the School of Pharmacy of the University of Maryland a portrait of his father, the late Charles E. Dohme, who was president of the Institution in its earlier years. The latter was president of the AMERICAN PHARMACEUTICAL ASSOCIATION in 1899.

Through the Courtesy of **Frank L. Black,** the ASSOCIATION has received from Dr. James C. Clarke, Baltimore, a hand scale with set of weights. Also, a framed receipted bill from the pharmacy of Dr. Hynson Jennings & Co., dated June 8, 1863.

[1] Dr. Barger delivered the inaugural address.

WILLIAM PROCTER, JR., AWARD.

John Uri Lloyd, senior member and past-president of the AMERICAN PHARMACEUTICAL ASSOCIATION, pharmacist, chemist, educator and author, was honored at a special ceremony, October 9th, at the Philadelphia College of Pharmacy and Science in recognition of his many and varied contributions to his chosen professions. To him was presented the Procter International Award in the form of a suitably inscribed gold watch.

This award is named in honor of William Procter, Jr. (1817–1874), a graduate of the Philadelphia College and long a member of its faculty, and editor of its *American Journal of Pharmacy*. William Procter, Jr.'s contributions to pharmacy and related sciences have won him undying fame.

The presentation of the award was made by Dean Charles H. LaWall and the award conferred by President Wilmer Krusen. The recipient responded with an informal address. Preceding the award, Chairman Samuel P. Wetherill, Jr., of the Board of Trustees, delivered an address and the exercises were opened with a biographical sketch of William Procter, Jr., by Prof. Ivor Griffith.

DEDICATION OF LILLY RESEARCH LABORATORIES.

Following an inspection by the Indianapolis Druggists' Association on Tuesday and a visit by the Indiana State Medical Association on Wednesday, the formal dedication of Eli Lilly & Company's new research laboratories took place on Thursday, October 11th, and was continued on the next day by inspection trips and addresses by guests of honor. Nearly one thousand guests were present and these came from all sections of the country, among them, **R. P. Fischelis**, president of the A. PH. A. The faculties and laboratories of many pharmacy schools were represented.

Featured on the program were the dedication address delivered by Eli Lilly, president of the company, and chairman at the dedication, and comments on research in manufacturing pharmacy by Josiah K. Lilly, chairman of the board of directors of the company.

"The Unpredictable Results of Research" formed the substance of an address by Dr. Irving Langmuir, famous American scientist and director of research for the General Electric Company. His address was followed by a review on "The Early Story of Insulin," Sir Frederic Banting of the University of Toronto. He was followed on the program by Sir Henry Dale, chairman of the National Institute for British Research, who delivered an address on the subject "Chemical Ideas in Medicine and Biology."

At a formal dinner tendered on Friday night by the Lilly organization at the Indianapolis Athletic Club, with J. K. Lilly functioning as toastmaster, the following speakers were heard: Sir Henry Dale, chairman of the National Institute for British Research; Dr. Elliott P. Joslin of Boston; Dr. George R. Minot of Boston; Dr. Frank R. Lillie of Chicago; Dr. Charles R. Stockard, N. Y.; Dr. George H. Whipple, Rochester; Dr. Carl Voegtlin, Washington; Dr. G. H. A. Clowes, director of the Research Laboratories.

WILSON & CO. LABORATORY WRECKED.

An explosion of undetermined origin in the pharmaceutical laboratory of Wilson & Co., Chicago practically wrecked the building and injured three persons slightly. The blast, which occurred in a basement boiler room near a storehouse of chemicals, blew out all the windows there, demolished a supporting post on the first floor and caused part of the second floor office and laboratory equipment to be precipitated into the basement. Immediately after the explosion, the basement was flooded with sulphuric acid from six shattered carboys.

OBITUARY.

Prof. John E. Groff, aged 80 years, for 40 years chief pharmacist of the Rhode Island Hospital and one of the founders of the Rhode Island College of Pharmacy, died at the hospital after a short illness. The deceased joined the staff of the hospital in June 1891, as chief pharmacist, and held that position ever since.

J. Percy Remington died suddenly in Portland, Oregon, September 17th, while on a visit to his sister there. He was the son of Professor Joseph P. Remington.

The deceased graduated from the University of Pennsylvania in chemistry, in 1898, and later came to the Philadelphia College of Pharmacy, where he received the degree of doctor of pharmacy. He was distinguished as an engineer and inventor and developed and patented many widely used mechanical devices for manufacturing processes.

SOCIETIES AND COLLEGES.

INTERNATIONAL CONGRESS OF PHARMACY.

The Twelfth International Congress of Pharmacy will be held in Brussels from July 20 to August 5, 1935. The general secretary is M. J. Breugelmans, 3 rue du Gouvernement Provisoire, Brussels.

THE NATIONAL ASSOCIATION OF RETAIL DRUGGISTS.

The National Association of Retail Druggists, in New Orleans, September 24th–29th, was largely attended; to a certain extent due to the interest developed preceding the convention and the attractions of the interesting city in which it was held.

Among the speakers of the N. A. R. D., aside from the officials who made illuminating addresses, relating to the subjects under their control, were the following: James H. Beal, E. F. Kelly, F. V. McCullough, H. J. Anslinger, U. S. Commissioner of Narcotics; James M. Doran, Administrator of the Distilled Spirits Institute, and W. Bruce Philip, of Washington.

Naturally, the code and its provisions was a subject of interest and entered into several addresses and reports. The report of the Form of Organization Committee was of great importance, because it was found necessary, if the N. A. R. D. is to continue representation on the National Retail Drug Code Authority, that the constitution and by-laws be altered to some extent.

While closer coöperation with the AMERICAN PHARMACEUTICAL ASSOCIATION was endorsed, merger of the N. A. R. D. and A. PH. A. was not approved. Dr. James H. Beal's address dealt with the subject. He gave a history of the organizations and detailed the activities of both.

Referring to the AMERICAN PHARMACEUTICAL ASSOCIATION, he said in part:

"The dominant purpose of the A. PH. A. in 1851 is its dominant purpose to-day. It considers the professional and scientific interests of pharmacy rather than its trade and commercial interests. It studies and reports upon commercial methods and practices, but only as necessary adjuncts to the proper conduct of a pharmacy.

"It devotes consideration to the scientific and professional interests not only of the retailer but to the professional and scientific interests of pharmacy as a whole. In fixing its requirements for membership it does not recognize any distinction between manufacturers, wholesalers or retailers, between proprietors or clerks, between professors in colleges of pharmacy and scientific research workers. What it does require of its members is an active interest in the advancement of professional and scientific pharmacy.

"Another striking feature of the A. PH. A. is that it is controlled by a House of Delegates, the majority of whose members come from state pharmaceutical societies, so that the A. PH. A. in fact is, and might very properly be called the 'Federation of State Pharmaceutical Associations.' "

RESOLUTIONS.

A large number of the resolutions applied to business matters and relations with other organizations, legislation, approval of the work of officers and the Association's activities. Among many resolutions the following are mentioned:

Opposing the filling of prescriptions by hospitals for non-patients and asking the American Hospital Association to urge its members to cease this practice.

Disapproving the use of the word "drugs" in newspaper stories when "narcotic drugs" are intended.

Praising the work of the "Old Apothecary."

Urging continuance of support to National Pharmacy Week and suggesting that retailers hold "open house" during this week.

Urging the issuance of a commemorative postage stamp in honor of the American Institute of Pharmacy.

Urging all associations to affirm and support a national fair trade act and recommending that all state associations seek the enactment of legislation similar to the California fair trade act.

A recommendation by President Powell that the association move its offices to Washington was approved by the finance committee.

The following officers were elected for the ensuing year:

Harvey A. Henry, of Los Angeles, was elected *President* of the Association. Other officers are as follows: *First Vice-President*, H. O. Chichester, of Macon, Georgia; *Second Vice-President*, Zack Kerrigan, of St. Louis; *Third Vice-*

President, M. V. Hardesty, of Louisville; *Secretary*, John W. Dargavel, of Chicago; *Treasurer*, Oscar Rennebohm, of Madison; *Executive Committee*, John Witty, of Portland, and Thomas Smith, of Wilmington, for three years each; Monte Powell, of Denver, for two years; and C. Fred Wright, of Boston, for one year.

FEDERAL WHOLESALE DRUGGISTS' ASSOCIATION.

Mutual and coöperative wholesale druggists were urged to coöperate individually with manufacturers, wholesalers and retailers in efforts to establish plans of price stabilization which benefit the retail druggist, in a resolution approved by the Federal Wholesale Druggists' Association at its nineteenth annual convention, held in Providence, R. I., September 16th to 19th. The action followed a discussion and members frankly and earnestly expressed their views on discounts, rebates and dividend allowances.

Hon. Harry J. Anslinger reported to the Association that uniform state narcotic laws had been enacted by Florida, Nevada, New Jersey, New York, Rhode Island, Kentucky, Virginia and South Carolina.

The following officers were elected: *President*, Harry Krupp, Philadelphia, Pa.; *Vice-President*, Edward Seiberling, St. Paul, Minn.; *Secretary*, Lee Williamson, Baltimore, Md.; *Treasurer*, George Raab, Providence, R. I.; *Members of the Executive Committee*, O. W. Osterman, Philadelphia, Pa.; T. F. Williams, Buffalo, N. Y.; Paul Pearson, Washington, D. C.; O. J. Cloughly, St. Louis, Mo.; Joseph Dreyer, Newark, N. J.

The Association formed a new committee on propaganda and invited buying which will study and direct procedure in connection with price stabilization. The members of the committee are J. J. Dreyer, Newark, N. J.; O. J. Cloughly, St. Louis; R. E. Lee Williamson, Baltimore; and F. T. Roosa, Cleveland.

NATIONAL WHOLESALE DRUGGISTS' ASSOCIATION.

Ogden L. Mills, Secretary of the Treasury under President Hoover, was one of the speakers at the meeting of the National Wholesale Druggists' Association. The convention at White Sulphur Springs, October 1st–5th, which was the 50th annual meeting, broke all precedents for attendance and interest.

Another speaker of the convention was Wheeler Sammons, director of the Drug Institute, whose address was based on difficulties encountered in efforts to bring peace to industry.

Dr. H. J. Ostlund of the University of Minnesota spoke on "The Distribution of Costs" in an effort to find out what it actually costs to have products reach the hands of the consumer.

Discussions on the codes and business affairs entered into program and President-Elect A. Kiefer Mayer made an analysis of the effect of the codes and how business must be shaped in order to successfully meet the demands.

Robert Lund presided as toastmaster at the banquet.

The following officers were elected for the ensuing year:

Honorary President, Andrew J. Geer, Charleston, S. C.; *President*, A. Kiefer Mayer, Indianapolis; *First Vice-President*, Dudwig Schiff, Los Angeles; *Second Vice-President*, W. W. Starkey, Pittsburgh; *Third Vice-President*, Edward S. Albers, Knoxville, Tenn.; *Fourth Vice-President*, Sam Dunlap, Jacksonville, Fla.; *Fifth Vice-President*, Charles Bergman, New York; *Members of the Board of Control*, William Ochse, San Antonio, Texas; Norman B. Livermore, San Francisco; and George Van Gorder, Cleveland, Ohio; *Executive Vice-President and Secretary*, E. L. Newcomb, 51 Maiden Lane, New York City; *Treasurer*, Title Guarantee & Trust Co., New York City; Washington *Representative*, W. L. Crounse, Washington, D. C.

AUSTRALASIAN PHARMACEUTICAL CONFERENCE.

Melbourne Centenary Meeting, January 16–23, 1935.

The biennial meeting of Pharmaceutical Associations of Australia and New Zealand will be held in Melbourne from January 16 to 23, 1935. Concurrently with the convention of the Associations, the meeting of the Australian and New Zealand Association for the Advancement of Science will take place. Pharmacists are represented in the latter Association by a section of their own—Section O, Pharmaceutical Science. Dr. Roy Gardner, of Dunedin, N. Z., is president of this section. It is in Section O meetings that the scientific and technical papers are read.

What is known as the Australasian Pharmaceutical Conference is the Pharmaceutical Associations meeting. At this meeting matters affecting the professional and business interests of pharmacists are discussed. A committee is now at work preparing the business agenda,

and it is expected that the 1935 meeting will be productive of good results.

MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY.

The division enjoyed well-attended sessions which were of unusual interest because of the quite general discussion which followed all papers on the program. Perhaps of chief interest was the Symposium on Medicinal Analysis. This was essentially an informal gathering. It offered ample opportunity for discussion between the various groups as to difficulties encountered in this field, and various methods and laboratory technique were brought out.

New officers of the division for the ensuing year were elected as follows: *Chairman*, John H. Waldo; *Vice-Chairman*, Walter H. Hartung; *Secretary-Treasurer*, D. L. Tabern.

AMERICAN REGISTERED PHARMACISTS' ASSOCIATION.

The Thirty-First Annual Meeting of the American Registered Pharmacists' Association was held in San Francisco, August 1st to 4th. The following officers were elected for the ensuing year: *President*, Albert C. Kasper, San Francisco; *First Vice-President*, A. A. Madsen, San Francisco Hospital, San Francisco; *Second Vice-President*, Alice M. Riordan, Los Angeles; *Secretary-Treasurer*, E. S. Berwick, San Francisco. *Directors:* Albert Keller, San Francisco; Robert Guild, Sacramento; William Gebhart, San Jose; Roy E. Hazlett, Jr., Davenport, Iowa.

CANADIAN PHARMACEUTICAL ASSOCIATION.

The Canadian Pharmaceutical Association held its twenty-second annual session in Saint John, August 6th–9th, and commenting thereon the *Canadian Pharmaceutical Journal* states that the meeting will be remembered as outstanding in the history of the organization.

Three guests are especially mentioned in the columns, namely, President R. P. Fischelis of the AMERICAN PHARMACEUTICAL ASSOCIATION, who brought greetings from that organization; Dr. R. E. Wodehouse, Deputy Minister of Pensions and National Health, Ottawa, who enlightened the members on the work being carried out by that department; Col. C. H. L. Sharman, Chief of the Narcotic Division, Ottawa, who discussed some of the difficulties of the division.

The *Canadian Pharmaceutical Journal* of September 15th comments on the address of President Fischelis in which he commended Canadian pharmacists on their unique organization which comprised all the druggists of the Dominion. He stated they should keep their forces consolidated and permit no division in their ranks.

It was deeply regretted that President H. D. Campbell of the Association could not be present on account of illness from which he is recovering. A letter of appreciation and greetings from him was read.

The following officers were elected for the ensuing year: *Honorary Presidents*, J. J. Kinley, Lunenburg, N. S.; E. Clinton Brown, Saint John, New Brunswick; Henry Groulx, Montreal, Quebec; W. G. Smith, Welland, Ontario; H. D. Campbell, Winnipeg, Manitoba; W. C. Black, Calgary, Alberta; *President*, J. H. Best, North Battleford; *Vice-President*, S. R. Balcom, Halifax, N. S.; *Chairman*, A. J. Wilkinson, Windsor; *Secretary*, R. B. J. Stanbury, Toronto.

The Pharmacy Week window installed by Reddin Bros., Charlottetown, won the F. A. Jacobs Trophy, which was presented during the meeting. The window featured prescription practice and a general and historical exhibit of iodine and several pharmaceutical processes.

Dean G. A. Burbidge spoke on "Pharmacy in the Drug Store." He outlined the methods adopted by the Province of Nova Scotia for the education of pharmacists, and referred particularly to the arrangements providing for certified clerks.

Secretary R. B. J. Stanbury, of the Canadian Pharmaceutical Association, and Secretary F. A. Jacobs, of the Ontario Retail Druggists' Association, participated in the functions of the Washington meeting of the A. PH. A., both are members and regular attendants at the annual meetings.

NATIONAL PHARMACY WEEK.

The *News Edition* of *Industrial and Engineering Chemistry* of September 20th, page 344, has an interesting article on this year's observance of Pharmacy Week. In order to complete the detailed report, the statement should have been included that Pharmacy Week had its inception at the meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION in 1924, as one of the recommendations of Robert J. Ruth in his address as chairman of the Section on Practical Pharmacy and Dispensing.

PURDUE PHARMACY WEEK OVER THE RADIO.

The story of pharmacy was told to the people of Indiana during National Pharmacy Week. Short musical programs accompanied the daily talks, the music was furnished by members of the several families of the pharmacy school staff and by the students of pharmacy.

The following were the speakers:

Dean C. B. Jordan, "Pharmaceutical Education;" President E. A. Ridgely, of the I. Ph. A., "What the Indiana Pharmaceutical Association Is Doing to Protect the Health in Our State;" H. W. Heine, "The Pharmacist and the Law;" Prof. H. G. DeKay, "The Druggist," and Prof. C. O. Lee, "The Inquiring Customer;" Prof. C. J. Zufall, "How Man Came to Use Drugs."

INSTALLATION OF THE PRESIDENT OF THE UNIVERSITY OF IOWA.

The AMERICAN PHARMACEUTICAL ASSOCIATION was represented by John Milton Lindly at the Installation Ceremonies of Eugene Allen Gilmore as President of the University of Iowa. State Senator Lindly functioned in the group of delegates of "Learned Associations and Foundations." He writes that when he graduated from the University the attendance numbered about 500, now about 8000; the great development was made largely during the presidency of the retiring president, Walter A. Jessup.

The attendance at the Inaugural Convocation was nearly 10,000, and the formal ceremonies were carried out in accordance with the University program, participated in by State bodies and institutions, the student body and representatives of other educational institutions. The name of Dean Wilber J. Teeters College of Pharmacy is the fourth in the Board of Deans.

PHARMACY TO-DAY.

President Robert P. Fischelis, of the AMERICAN PHARMACEUTICAL ASSOCIATION, opened Pharmacy Week with a radio address on "Pharmacy To-Day." The opening message stressed the importance of health and the service of pharmacy contributory thereto.

The speaker referred to the care necessary in pharmaceutical practice and gave an example of the possibility of error through carelessness and incompetency. The activities of the several divisions of the drug industry were depicted and reference made to educational and legal requirements governing pharmacy. The address was comprehensive, interesting and well received.

AERIAL POLLEN SURVEY.

An aerial pollen survey was inaugurated by the Philadelphia College of Pharmacy and Science on September 20th, a ceremony marked the beginning of this survey. Endorsement of the plan and commendation was offered at the meeting by Dr. Theodore B. Appel, Secretary of Public Health of Pennsylvania; Dr. J. Norman Henry, Philadelphia Health Director; Dr. Arthur C. Morgan, Secretary of the Pennsylvania Board of Medical Licensure; and Dr. Randle C. Rosenberger of the Jefferson Medical College.

The surveys are to be conducted daily and the collection made by air-plane, from the entire metropolitan area of Philadelphia and a section of southern New Jersey extending seaward twenty miles. A model of one of the air-planes to be used in the survey was presented to the College by Dr. Henry K. Seelaus who, with Dr. A. H. Zifferblatt, is in immediate charge of the work. Devices for collection of air samples during flights were designed and constructed in the college Engineering Department, under the direction of Frank N. Moerk. The air-planes necessary for the flights have been donated by Richard Mark, a patient of Dr. Seelaus, and Dr. Zifferblatt, who is a sufferer from hay fever.

CANADIAN PHARMACY WEEK WINDOW.

Friends of the late George E. Gibbard, founder of the Canadian Pharmaceutical Association, have created a fund whereby the winning pharmacy window receives a Canadian cup and retains it for one year. The winner will be presented with a miniature to keep permanently. The window is to be a professional display. Photographs of the window are to be sent to the provincial chairmen.

Announcement of the winner will be made before the close of the Canadian Pharmaceutical Association 1935 convention and if the winner is present the trophy will be formally presented.

Samuel L. Hilton has added to his contributions to the Library, A. PH. A., by giving twenty volumes of the JOURNAL, A. PH. A., U. S. P. Circulars, Treasurer's financial reports, N. F. Bulletins, etc.

Charles H. LaWall has donated a number of photostat copies of historical records, among them page photostats of Charles Marshall's "Waste-Book."

DEDICATION OF THE CHEMISTRY BUILDING IN PARIS.

Ceremonies in connection with the dedication of the Chemistry Building in Paris were held on October 19th and 20th. The program provided for an address by President M. Albert Lebrun of France; a visit to the building, and a banquet in honor of the delegates and visitors.

CALIFORNIA COLLEGE OF PHARMACY.

The Board of Regents of the University of California has announced that it has assumed direct control of the California College of Pharmacy. The College has been affiliated with the University since 1875, but had its own board of trustees and business managers.

LEGAL AND LEGISLATIVE.

BOARD OF SEVEN DIRECTS NRA.

On September 28th, the National Industrial Recovery Board, created by Presidential Executive Order, took over the duty of administering NRA. The Board is composed of S. Clay Williams, Chairman; Leon C. Marshall, Executive Secretary; A. D. Whiteside, Sidney Hillman and Walton Hamilton. Blackwell Smith and Leon Henderson were named Legal Adviser and Economic Adviser, respectively, to serve ex-officio as members of the Board. At its first meeting, the Board announced that there would be no drastic changes in either policy or personnel but that such alterations as experience proves to be necessary will be developed gradually. It reappointed Col. George A. Lynch as Administrative Officer, empowering him to sign such documents as do not require the personal signature of the President, and to continue supervision of the entire administrative machine of NRA.

CODE AUTHORITY BUDGET.

Public hearing will be held October 23rd, at the Raleigh Hotel, Washington, on the proposed Code Authority budget and basis of contribution for the retail drug trade.

Amendments to the mandatory assessment clause and amendments to permit incorporation of the Code Authority and of local and metropolitan authorities, also will be discussed.

The proposed budget totals $50,000.00 for January 1, 1934, to January 1, 1935. It is proposed that each local and metropolitan drug establishment contribute up to $1.00 per employee per year, and that of this sum the National Retail Drug Code Authority receive one dollar per retail drug establishment.

CODE APPROVED FOR HAWAIIAN RETAIL CODE.

The National Industrial Recovery Board, on October 15th, approved a code for the retail trade in the Territory of Hawaii. This code will affect some 2800 establishments employing about 15,000 people. It will become effective October 29th.

This is the first approved code to apply solely to the Territory.

Supplementary schedules appended to the code contain special provisions for retailers of drugs and allied products; food, groceries and their allied products; music and radio; electric refrigeration; jewelry and allied products; and photography and photo-finishing.

The code for Hawaii follows the mainland retail code closely. The hours and provisions are identical, establishing a basic maximum workweek of 40 to 48 hours, depending on population and hours of store operation. Minimum wages follow the same scale but are lower for Hawaii than on the continent, ranging from $9.00 to $12.00 a week.

The Board's order approving the code specifically exempts members of the trade from the provisions of any other code, to the extent they are engaged in retail trade in Hawaii. It also stays the minimum wage provisions as to outside salesmen, and as to employees of retail drug establishments who spend 60 per cent of their time delivering merchandise outside of the shop.

The code applies to "all selling of merchandise to the consumer and not for resale" in the Territory of Hawaii, but selling milk and dispensing of drugs by doctors in the legitimate practice of their professions are exempted.

Administration of the code is entrusted to a Territorial Code Authority made up of the chairmen of the County executive committees of the Retail Association of Hawaii. The county executive committees are to act as County Code Authorities. The trade practice provisions and the schedules for the various divisions of the trade follow very closely the rules approved for those trades on the mainland.

WILLARD L. THORP APPOINTED ASSOCIATE ECONOMIC ADVISER.

The National Industrial Recovery Board, on October 15th, announced the appointment of Dr. Willard L. Thorp as associate economic adviser to the National Industrial Recovery Board in the Division of Research and Planning. Dr. Thorp will be the division's representative and chairman of the Advisory Council.

Dr. Thorp has been professor of economics at Amherst College and a member of the research staff of the National Bureau of Economic Research, Inc. Since coming to Washington as a member of the Committee on Government Statistics he has served as director of the Bureau of Foreign and Domestic Commerce, and is now director of the Consumers' Division of the National Emergency Council and a member of the Federal Alcohol Control Administration, the Committee on Mineral Policy and the Industrial Resources Committee.

PHILIPPINES TO EXCLUDE FOREIGN PHARMACISTS.

Following the advice of the Filipine Pharmacists' Union, the Filipino Pharmacists' Examination Commission, on July 20th, adopted the following two resolutions:

1. Practice of pharmacist should be limited to Americans and Filipinos.

2. Owners of dispensaries should be limited to Americans or Filipinos who are graduates of a school for pharmacy.

It was further resolved that handling of drugs should be made only by Americans or Filipinos who have resided in the country for at least one year and that no license should be given to those who have no qualifications stated above after next January.—*Japanese Retail Druggists.*

TRADE-MARKS IN MANCHOUKUO.

During the nine months that elapsed since the government of Manchoukuo enacted the trade-mark law up to the end of July a total of 14,988 applications for trade-marks were applied for. The principal applications have been from Japan, 12,010; Germany, 944; Great Britain, 879; United States, 459; France, 219.

ITALIAN NARCOTIC RULES.

The new regulations concerning narcotics, as published in the *Gazzetta Ufficiale*, provide that penalties in the form of imprisonment for from one to three years and a fine of not less than 1000 lire ($84.00) shall be imposed on any person who grows *Papaver somniferum* secretly, who produces crude opium or who collects or carries on traffic in opium capsules, leaves of coca and/or Indian hemp, writes the Italian correspondent of *The Journal of the American Medical Association.*

No public or private place may be used for the gathering of persons who indulge in the use of narcotic substances; not only the keeper of the place but also the addicts are subject to a fine and/or imprisonment.

Persons authorized to sell narcotics may not dispense them without a medical prescription nor to persons whose identity is unknown. Morphine, diacetylmorphine, cocaine and their derivatives may not be sold other than in the form of an ointment or a solution. The medical prescription must be written with ink or indelible pencil and according to a special form; it must contain a general description and the address of the patient, the amount of the dosage written out in full, and directions as to the manner and time of administration.

ALABAMA LEGISLATION.

Attorney-General Thomas E. Knight, of Alabama, has ruled that "The terms 'patent' or 'proprietary' medicines as in this act shall be interpreted to mean those package medicinal products advertised to the general public for certain medication, and not those products or preparations advertised to physicians under copyright or trade names to be prescribed; those products recommended by the U. S. P. and the N. F., except those items which should have been or may be classified as household remedies or those products or preparations which from their natural and known effects should have been dispensed, sold or prescribed for use by the public except upon the prescription or advice of a licensed physician or licensed pharmacist."

TEXAS.

Bill Introduced Texas H. 55-XXX proposes to forbid the sale of barbituric acid "derivatives and compounds thereof under any copyrighted or chemical name," except on the prescription of a licensed physician. The proposed act, however, is not to affect the sale of such drugs by wholesale drug houses to retail pharmacists or to physicians. A licensed physician is free to dispense these drugs, but, apparently, will be able to buy them from retail pharmacies only on prescription.

SALE OF ACETYLSALICYLIC ACID TABLETS.

The Federal Trade Commission has issued an order to the Bayer Company, Inc., New York, to cease and desist from using unfair competitive practices in the sale of its acetylsalicylic acid tablets. The company is directed to cease using language in its printed advertising or radio broadcasting stating or giving the impression that "aspirin" is a trade-mark of the Bayer Company, however; this order does not apply to advertising on packages to be sold in foreign countries in which the word "aspirin" has been held to be the Bayer Company's valid trade-mark. A list of seventeen representations are given in the commission's order, which the company is not to use unless properly qualified, limited or explained. Among them are such expressions as "It cannot harm the heart," "Bayer aspirin is always safe," "Take Bayer aspirin for any ache or pain, and take enough to end it. There is no harm in its free use," "Genuine Bayer Aspirin tablets promptly relieve headaches, neuritis, colds, toothache, neuralgia, sore throat, lumbago, rheumatism." The order is not to be construed as preventing the company from making proper therapeutic claims or recommendations based on reputable medical opinion or pharmaceutical literature, it was stated. The third prohibition in the order is one providing that the company shall not in any way represent that acetylsalicylic acid tablets manufactured by other firms are counterfeit or spurious. The company waived a hearing and did not contest the proceeding of the commission.—From *Jour. A. M. A.*, 10/13/34.

BOOK NOTICES AND REVIEWS.

Organic Chemistry or Chemistry of the Carbon Compounds. By VICTOR VON RICHTER. Volume 1: Third English Edition, 1934. 790 pages. Published by P. Blakiston's Sons & Company, Philadelphia, Pa.

This is the sixth edition in the English language, being the third American edition. The system of presentation followed in the previous German, English and American editions has been retained. The first volume of this series deals with the aliphatic series only. The order of presentation moves progressively from the hydrocarbons (1) to the halogen derivatives (2), the monohydric alcohols, aldehydes, ketones and carboxylic acids (3), the dihydric alcohols and their oxidation products, (4), to the trihydric, tetrahydric, pentahydric, hexa- and polyhydric alcohols, each group being considered with its oxidation product. Short chapters then follow, dealing with the carbohydrates, protein, chlorophyl, bile pigments, sterols and enzymes.

It has been interesting to compare this 1934 publication with the third American translation of the eighth German edition published in 1913. The same encyclopedic arrangement of products is observed. The same presentation of material believed to be more important in large print, and material believed to be of lesser importance in finer print has been followed. Many paragraphs of the 1913 publication have been reprinted without change in 1934. The information presented has been brought up to 1932 on some subjects, but on others most recent references are to publications in the nineteenth Century. Many references are to German or French articles which are not readily available. Some specific developments have been stressed, such as the electronic theory of valency, and the parachor.

The book will still prove useful in the orderly presentation of organic chemistry. However, it needs to be supplemented in many points in order to harmonize with teachings on polar molecules, etc. This book fills an intermediate rôle between the elementary texts and the encyclopedias, such as Beilstein.—JAMES C. MUNCH.

Bacteriology and Sanitary Science. By LOUIS GERSHENFELD, Ph.M., B.Sc., P.D., Professor of Bacteriology and Hygiene and Director of the Bacteriological and Clinical Chemistry Laboratories in the Philadelphia College of Pharmacy and Science, Philadelphia. Price, Limp Leather Binding, $4.50. Publishers, Lea & Febiger.

Gershenfeld's second edition of Bacteriology and Sanitary Science is an interesting and authoritative treatise which covers both the technical and practical aspects of many of the important subjects on which the pharmacist has opportunity of offering sound advice. In addition it contains a concise statement of many techniques which are useful to the up-to-date pharmacist in his own work.

Obviously, a book devoted to such a large field of knowledge and practice cannot deal with each of the basic sanitary sciences—bacteriology, immunology, parasitology, sanitary engineering and the production of biological products—in complete detail. Therein lies its virtue. The author has accomplished the very difficult task of separating the specialist's chaff from the pharmacist's wheat. The book is recommended to students and to registered pharmacists.—JOHN M. HANKS.

New and Nonofficial Remedies.—The American Medical Association has issued a supplement to New and Nonofficial Remedies for 1934. This supplement contains descriptions of the articles which have been accepted by the Council on Pharmacy and Chemistry of the American Medical Association since January and do not appear in the volume prepared for 1934. The Council states that the acceptance of an article does not necessarily mean a recommendation, but as far as it is known, the preparation complies with the rules adopted by the Council. Criticisms and corrections to aid in the revision of the next volume, before publication, are asked for.

Burroughs Wellcome Research Institution and Affiliated Research Laboratories and Museums have issued a beautiful bound illustrated booklet of the exhibits at the Chicago Exposition. Excellent half-tones of the ceremonies at the Corner Stone Laying of the Wellcome Research Institution grace the introductory pages. Lists of guests and press reports follow.

Whitla's Pharmacy, Materia Medica and Therapeutics. William Wood & Company, Baltimore (Bailliere, Tindell & Cox, London, England). 645 pages. Price $4.25. Sir William Whitla, in the preface to the first edition (1881), stated that the aim of the work was to give to the student of medicine such information in a concise form, as he generally has to sift out of two or more of the larger manuals. The author was actuated by the feeling that pharmacy is one of the most important sections of Materia Medica; he believed that a knowledge of it should be an essential accomplishment of every educated physician. It is evident that the author prepared the treatise, primarily, for physicians.

Dr. J. A. Gunn, reviser of this edition, 12th, states that an effort has been to retain observations made by the original author which were based upon his own clinical experience, and the actual text has been preserved wherever possible; extensive alterations have been necessary by the appearance of the new British Pharmacopœia. Dr. Gunn is professor of Pharmacology in the University of Oxford and his assistants in the revision, H. Berry, is head of the Department of Pharmacy, Birmingham Central Technical College and member of the Board of Examiners of the Pharmaceutical Society of Great Britain, and J. Clifford Hoyle, M.D., of the London Hospital, is Examiner in Pharmacology of the University of Cambridge.

The authors apply the term "Materia Medica" to the description of the physical characters of remedies, their origin, source, distribution, chemical composition and the methods by which they are obtained, collected, preserved, etc.; "Pharmacy" to the methods by which they are prepared and made ready for administration; "Pharmacology" to the science of their action on a healthy organism and "Therapeutics" to their application in the treatment of disease.

Eight pages are given to Treatment in Cases of Poisoning; the other divisions of the Book are: Part 1, Pharmacy; 2, Prescription Writing; 3, Materia Medica of the British Pharmacopœia; 4, Therapeutics; 5, Non-Official Remedies. Conciseness features the work and serves its purpose; without adverse criticism it may be said that other works on pharmacy are better adapted to the needs of pharmacists, but the text is well arranged and the matter well presented for the needs of physicians, and it may be said that if the volume was part of more libraries prescription writing would be improved.

The British Pharmacopœia under "authorized contractions" uses gram and then states that in order to avoid confusion the symbol "G" should be used as the contraction for "gramme." In Whitla, no attention is given to either contraction, "gm." is used; these variations are apt to confuse physicians in writing prescriptions.

Considering the work as a whole, it serves a useful purpose for British physicians and pharmacists; for the American profession it has value as a reference book; more extended references could have been made to both professions and to legal phases applying to the practice of the professions.